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SHORT COURSE OF LECTURES ON ORGANIC PHOSPHORUS COMPOUNDS

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TABLE OF CONTENTS

JPRS: 5598
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/Following is the complete translation of the book by F. V. Rodionov entitled "Kratkiy Kurs Lektsiy po Fosfororganicheskim Veshchestvam" (English version above), Kiev, 1959, pages 3-76./

A brief course of lectures on organic phosphorus compounds designed for physicians and workers in the medical service of the MPVO /Antiaircraft Defense/. It contains brief information on the pathogenesis, clinical aspects and therapy of intoxications with organic phosphorus compounds. In the lectures the main data are also presented concerning the organization of medical care and antichemical protection from injuries with these substances.

Foreword

The present short course of lectures on organic phosphorus compounds has been written by a group of workers of the Ukrainian Sanitation-Chemical Institute with consideration of the data published in the literature and designed chiefly for physicians and workers in the medical service of the MPVO /Antiaircraft Defense/. Because of this no information is given concerning the chemistry of organic phosphorus compounds.

The significance of organic phosphorus compounds at the present time is exceptionally great, and, as is well known, is not limited simply to the possibility of utilization of some of them as war gases (Sartori). They have been used extensively in the national economy as powerful insecticides as well as in the capacity of drugs.

The foreign literature devoted to organic phosphorus compounds is very expensive at the present time; this applies particularly to articles in the periodical scientific press. At the same time, there are no monographs in which the current status of the problem of the pathology, clinical aspects, prophylaxis and therapy of injuries by these substances are given completely and in a form available to

the physician.

The lectures being brought to the attention of the readers do not claim to be a monographic presentation of the entire material connected with problems of the toxicology and the sanitation-chemical protection from injuries by organic phosphorus compounds. Here, only the most important and essential material from what has been published on these problems is presented so as to give physicians and workers in the MPVO the main information which they need.

For convenience, the material has been presented in the form of four lectures which are connected with one another. Because of the brevity of these lectures it has not been possible in a number of cases to give an exhaustive presentation of the problem and we have had to be limited to references to various authors. Therefore, the authors have considered it necessary to give also a bibliography which they used in preparing the data for these lectures.

As a whole, the material being presented can serve as a brief reference for familiarizing physicians and workers of the medical service with the principles of toxicology and sanitation-chemical protection against intoxications with organic phosphorus compounds.

Professor P. V. Rodionov

First Lecture

Introduction

The use of chemical compounds for military purposes is nothing new. However, a number of the specific characteristics inherent of war gases (OV), gives them certain advantages compared with atomic and other attack weapons (like, for example, the injury only to enemy personnel with complete preservation of the materiel belonging to him) andaccounts for the considerable military potential of chemical weapons. Therefore, there is no basis for excluding the possibility of an attempt by an aggressor to use war gases as mass attack weapons against the population in case he unleashes a new war. This circumstance gives rise to the need for preparing the entire medical service personnel of the MPVO for antichemical protection.

Of all the war gases known at the present time the class of organic phosphorus war gases has acquired the greatest significance now. This is explained by the fact that the latter have a number of characteristic properties which give them advantages over other war gases. Thus, they are distinguished by their high degree of toxicity, which exceeds the OV previously known. The presence of negligibly small quantities of the vapors of these compounds in the air is sufficient to

produce the rapid occurrence of serious injuries, sometimes with a fatal outcome. They possess the capacity of penetrating into the respiratory tract, skin and digestive tract, thereby very rapidly exerting a pronounced general toxic effect without a local reaction. Characteristic of them is a difficulty of detection as well as a complexity of the organization of timely medical care for those afflicted because of the rapidity of the general toxic effect and the severe degree of injury. However, here, not only detection but also effective medical care are entirely possible. Finally, the raw material for the preparation of these substances is comparatively readily available, and the method of production of them is relatively cheap. All this makes the organic phosphorus compounds one of the most important groups among the modern war gases and accounts for the need for an extensive familiarization of medical service workers of the MPVO with this group of substances. The present lectures are devoted to this. The material of them includes the principal problems of toxicology of injuries by organic phosphorus compounds, the main problems in rendering medical care, antichemical protection, detection as well as sanitary processing and degassing. The lectures are designed for medical service workers of the MPVO at large.

Historic Review of the Occurrence and Development of Chemical Weapons

The history of development of chemical attack weapons shows that chemical agents were used even in the past with the aim of putting as large a number of persons out of commission as possible,

demoralization of military units and producing difficulties in defense organization. It is well known, for example, that even in the Peloponnesian War (431-404 B.C.) the Spartans specially burned a resin so as to use the smoke for fighting against their enemy. Much later, in the 19th Century the English suggested the use of smoke grenades for fighting against Russian troops. Therefore, the idea of chemical attack weapons is very old, but the use of chemical agents as war gases has become possible on a broad scale only in the 20th century, when the productive forces of society have reached a certain level of development.

Four periods may be distinguished in the development of military toxicology. The first period includes the time of the First World War (1914-1918), when Germany, preparing to change the map of the world, created a powerful chemical industry and treacherously used non-persistent war gases at first on the Western (22 April 1915) and then on the Eastern Fronts (31 May 1915). The further development of chemical attack weapons advanced the problem of looking for persistent, non-volatile and strongly toxic substances which might contaminate the human environment, food products and military technical equipment for a long time. Mustard gas, which was used shortly afterwards by the German army (13 July 1917), answered all these requirements, which put it in one of the leading places among the most dangerous OV. The appearance of mustard gas led to the rapid perfection of methods of protection of respiratory organs, vision

and of the skin.

The experience of the First World War clearly demonstrated the advantage of mustard gas, from which the troops of the Allies lost eight times more persons in a comparatively short time than from all the other war gases together.

The second period of development of the toxicology of OV (1918-1939) is characterized by intensive preparation of the capitalistic governments for a new world war, mainly directed against the Soviet Union.

During this period, the synthesis of substances with a cutaneous and general toxic effect was developed most vigorously. At first, lewisite, which was equal to mustard gas in its strength but had a much smaller latent period of toxic effect and produced injury to the body much more rapidly, was put on supply as a weapon, and then, phosgenoxime, a substance with a strong cutaneous, asphyxiant, irritative and general effect from absorption. In the last few years of this period trichlortriethylamine was put on the military supply of foreign armies; this substance was capable of acting on the living organism in a manner similar to sulfur-containing mustard gas with the difference only that it produces a more severe injury to the central nervous system.

The third period of development of the toxicology of the OV includes the time of the Second World War (1939-1945), at which time the capitalistic countries accumulated "new" war gases -- the organic

phosphorus compounds (Sartori), in addition to the "old" war gases, which in the strength of their effects on the central nervous system had no equals.

Surrounded on all sides by enemies, the Soviet Union, during the period of the building of Socialism, was very much interested in increasing its own military might and, therefore, made a systematic study of problems of the clinical aspects and pathology of the war gases, perfected methods of individual protection, worked out the most rapid methods of detection and degassing for the new war gases, thereby creating a clear-cut system of organization of medical first aid, evacuation and stage therapy of the afflicted persons.

During the Second World War the German army was completely prepared for and intended to use chemical weapons, but this did not occur simply because of the power of the Soviet Union and the victorious offensive of Soviet troops.

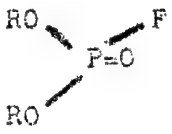
The fourth period of development of the toxicology of the OV (from 1945 through the present) is characterized by intensive research by chemists and toxicologists in the United States and England, directed at obtaining new rapid-acting, highly toxic war gases, affecting the central nervous system. During the post-war period a new trend also occurred -- the toxicology of radioactive substances. Its importance is entirely obvious, if we take into consideration the fact that after the explosion of atomic and hydrogen bombs ionizing radiation occurs (gamma-rays and neutrons) in addition to the other injurious factors.

In addition, in the military equipment of foreign armies there are specially prepared chemical agents which contain radioactive atoms (military radioactive substances -- BRV) designed for affecting troops and the peaceful population and for prolonged contamination of the terrain, buildings, air and food products.

The appearance of new mass attack weapons led to a change in the tactics of all the MPVO services, but it has not in any degree decreased the significance of chemical weapons. At the same time, the possibility of production of the latter in large quantities with the presence of a highly developed, powerful air force and other attack weapons have considerably increased the prospects of using war gases in modern warfare. Therefore, the interests of antichemical defense require the persistent study of new war gases, a systematic acquaintance with the methods of their detection, degassing and protection against injury from them.

Physicochemical Properties and the Toxicity of Organic Phosphorus Compounds

Among the new OV, possessing a high degree of toxicity and predominant effects on the central nervous system, a number of organic phosphorus compounds well known as fluorophosphates occupies a special place. These compounds were discovered by Lange and Kruger, who in 1932 synthesized a series of organic phosphorus compounds with the following general formula.



This class of compounds is constituted by the diethers of fluorophosphoric acid, substituted amides of fluorophosphoric acid, and other compounds similar to them. Interest in these substances has been brought about by their high degree of toxicity, which exceeds hydrocyanic acid. For example, the presence of negligibly small quantities (1:10,000) in the air of the vapors of these compounds is sufficient to cause the rapid death of animals. Lower concentrations (1:100,000) cause a prolonged disturbance of vision, associated with miosis and loss of accommodation. Typical representatives of this class of compounds are the ethyl ether of dimethylamidocyanphosphoric acid, well known by the name of tabun, and sarine, the acid fluoride of the isopropyl ether of methylphosphinic acid. Both tabun and sarine represent fluids with a slight odor, readily soluble in gasoline and acetone; poorly soluble, in water. Tabun has a specific gravity of 1.097 and a boiling point of 103-104° (at 10 mm of mercury); sarine, a specific gravity of 1.094 and a boiling point of 50° (at 12 mm of mercury).

In the investigation in the relationship between the effect and the structure of organic phosphorus compounds it was determined that the maximum degree of toxicity is shown by compounds containing a branched aliphatic radical. When the fluorine in them is

substituted by other groups or even by another halide the toxicity decreases sharply. The temperature of the surrounding medium, the age of the person affected, the condition of the nervous system, the area of the skin on which the substance falls all have an influence on the course of intoxication by organic phosphorus OV. If there are scratches or other defects in the skin the signs of intoxication occur very quickly.

All the representatives of this group of compounds possess a pronounced general toxic effect, which is manifested after entrance through the skin, inhalation of the vapors or other methods of application. These substances do not exert any local irritative effects. Drops of the OV are absorbed into the body without changing the skin. Along with cutaneous application, the inhalation method of using organic phosphorus compounds is an entirely possible form of application under military circumstances, because their physicochemical properties make it possible to create a high concentration of OV in the air. By comparing the data which characterize the toxicity of certain organic phosphorus and other OV, it may be noted that the toxicity of the former on inhalation exceeds the toxicity of the other OV by many times. The toxicity of the organic phosphorus compounds is also great when they enter the stomach along with the food and water.

Therefore, the high degree of toxicity of organic phosphorus compounds after their effect through the skin and particularly through

the respiratory tract, the difficulty of detection of them and the ease of production of them have advanced the organic phosphorus compounds to one of the important places among the modern OV (Sartori).

The Mechanism of the Effect of Organic Phosphorus Compounds and of The Transformation of Them in the Body

The pathological processes which develop in the body after the entrance of the toxin are produced by the toxigenic reactions occurring between the toxin and the blood, and between the toxins and the body's tissues. As a result of this the normal structure and properties of the biological substrate which interacted with the toxin are impaired, the result of which is a disorder in the functions of various organs and systems of the body. After the entrance of war gases into the body, including the organic phosphorus compounds, the blood carries them to the tissues. The role of the blood thereby does not consist only in the mechanical transfer of the toxin to various tissues. As a result of the presence of organic phosphorus compounds in the blood the major portion of them is detoxified. After a ten-minute contact with blood, the acid fluoride of the isopropyl ether of methylphosphinic acid (PFP) is detoxified even in doses which exceed one lethal dose. The injection of such blood into mice does not produce any intoxication in them. In experiments in which the blood was replaced by Ringer-Locke solution, the lethal dose of the toxin was considerably decreased. On a more detailed investigation it was shown that not only whole blood but also its constituents possessed the

capacity of detoxifying organic phosphorus compounds, whereby plasma is the most active.

In the study of the nature of this detoxifying effect it has been determined that in the body's tissues there is a special enzyme which catalyzes the hydrolysis of diisopropylfluorophosphate (DFP), as a result of which the latter loses its toxicity. The hydrolysis occurs at the fluorophosphate linkage, as a result of which hydrofluoric acid is split off (Mazur, 1946). Mazur described a number of properties of this enzyme, partially purified it and gave it the name of phosphofluorase. In 1953, Aldridge found an enzyme in the blood serum which hydrolyzes para-nitrophenyl phosphate (phosphacol).

Nevertheless, despite the data presented, the existence of such an enzyme in the tissues cannot be considered proved, because no compounds are known in the organism which possess a fluorophosphate linkage and which can serve (in the body) as a substrate for it.

The detoxifying power of tissues in the organism varies. Thus, in the blood, spleen, suprarenal glands the detoxification of organic phosphorus compounds occurs in a very active manner; cerebral and muscular tissue detoxify the organic phosphorus compounds to a very slight degree. It is possible that this is the cause of the fact that nervous tissue is the central place for the effect of these toxins, despite the fact that from the study of their distribution in various tissues it has been shown that they accumulate in the brain in relatively small quantities. Despite the detoxification, part of

the organic phosphorus compounds manages to pass from the blood into the tissues, whereby the entrance into various organs occurs with different rates of speed also. It should be kept in mind that even with the destruction of the organic phosphorus compounds by blood and tissues the former do not completely lose their toxic properties, and the decomposition products formed thereby possess varying degrees of toxicity.

Under conditions of the biochemical experiment it has not been possible to detect any reactions between the organic phosphorus compounds and carbohydrates or lipids containing reactive carboxyl groups. However, after treating proteins with organic phosphorus compounds which include fluorine, the latter can be detected in the protein bodies, but it has been difficult to determine the chemistry of this reaction. Thus, it has not been possible to show any reaction of the organic phosphorus compounds with the most active protein groups -- the amine and sulfhydryl groups. The inactivation of certain enzymes, which, as is well known, are protein substances in their nature, serves as proof of the toxic effect of organic phosphorus compounds on proteins.

Considerable attention has been given also to the study of the effect of organic phosphorus compounds on various types of metabolism. Here, distinct disturbances have been detected in the carbohydrate and cholesterol metabolisms. For the purpose of elucidating the mechanism of action of organic phosphorus compounds on the body

a study was made of their effects on various enzyme systems, which turned out to be very different. Among the enzymes which are relatively insensitive to the effect of organic phosphorus compounds are peroxidase and cytochrome oxidase (Webb, 1948). According to Webb's data, the alkylfluorophosphates do not influence the activity of carboxylase or carbonic anhydrase.

Along with enzymes which are insensitive to organic phosphorus compounds sensitive enzyme systems have been found the activity of which falls sharply after the effect of negligible quantities of these toxins. Thus, the activity of trypsin and chymotrypsin decreases distinctly under the influence of DFP (Jansen and others, 1949). Other phosphorus-containing toxins also suppress the catalytic properties of these enzymes, but their inhibitory effects develop more slowly (Hartey, Bang, Killy and others, 1950).

The most sensitive enzymes are cholinesterase of all the tissues and lipase, with the exception of pancreatic lipase. The sensitivity of the blood serum lipase to organic phosphorus compounds was shown by Bloch in 1943. Webb and Boursnell in 1949 published data concerning the power of DFP considerably to inhibit the liver esterase and shortly after confirmed this by experiments with the purified enzyme. The effect of a marked suppression of the activity of cholinesterase in the blood and in the tissues after intoxication by organic phosphorus compounds was determined by many investigators (Needham and Dixon, 1946); Mackworth and Webb (1948); Kelly and

Gilman, Harvey, du Bois, Dlull, Saberno and Cook, (1949). According to the data of the majority of authors this cholinesterase inactivation is irreversible (Brauer and others, 1947; Aldridge, 1950). Nevertheless, certain data of other studies speak for the fact that during the initial phases the inhibited cholinesterase activity can be restored (Nachmansohn, Rothenberg, Feld, 1947). The high degree of sensitivity of cholinesterase to organic phosphorus compounds, which is maintained for a long time, made it possible to advance the hypothesis of the accumulation of acetylcholine in the intoxicated organism, which was confirmed by the similarity of the pharmacological effect of the latter and of organic phosphorus compounds. However, such a method of dealing with the mechanism of action of organic phosphorus toxins gave rise to lively polemics. The proponents of the anticholinesterase mechanism attempted to link the development of the signs of intoxication caused by these substances with inhibition of cholinesterase activity. Actually, it was possible to show that in animals intoxicated with organic phosphorus compounds the cholinesterase activity was considerably reduced in all organs, particularly in the central nervous system, by comparison with the controls.

A parallelism has been noted by certain investigators between the toxic effect of some organic phosphorus compounds, the miotic effect, and the degree of inhibition of cholinesterase activity (Mackworth and Webb, 1958). Finally, it has been possible to show a certain relationship between the degree of depression of cholinesterase

and the severity of the injury (Freedman and Himwith, 1948). Numerous data have indicated the fact that death of the animals intoxicated with organic phosphorus compounds frequently occurs with a complete depression of the cholinesterase activity in the brain (Euler and Swanberg, 1930; Hawkin and Mendel, 1947; Mazur and Bodansky, 1946; Nachmansohn and Feld, 1947). These facts are in good agreement with the data concerning the effect of organic phosphorus compounds on various organs, where in the majority of cases the phenomena of impairment of function can be associated with the delayed decomposition of acetylcholine and its accumulation in the tissues. Thus, for example, in intoxicated animals a slowing of the cardiac rate is observed with an increase in the tone and motor function of the gastrointestinal tract, spasm of the bronchi, causing difficulty in respiration, salivation and lacrimation. The sensitivity of all these systems to acetylcholine is markedly increased thereby.

During the course of the further study of the effect of organic phosphorus compounds on the body, however, other facts were accumulated. Thus, specifically, the data concerning the obligatory parallelism between the degree of suppression of the activity of cholinesterase and the toxic effect of organic phosphorus compounds have not been confirmed (Jones, Meyer, Kurel, 1948; Kahlson, Uvnas, 1938).

Here, it was shown that the increase in sensitivity to acetylcholine does not necessarily depend on the anticholinesterase

effect (MacNamara, 1954), because sometimes a less toxic substance, for example, DFP, causes a more marked depression of cholinesterase than a more toxic substance, for example, tetraethylpyrophosphate. Recently, it has been determined that DFP causes the death of axolotls in the phase of development where the body still does not contain any cholinesterase (Karzmar, 1954). In 1949, G. D. Smirnov and G. M Turpayev showed that depression of cholinesterase in atropinized animals is not associated with death of the animals.

Therefore, on a par with the convincing data speaking on behalf of the anticholinesterase mechanism of action of organic phosphorus compounds, there are proofs of the fact that the entire complicated mechanism of action of these toxins on the body is not limited simply to an effect on this enzyme. Therefore, the anti-cholinesterase effect of organic phosphorus compounds may be regarded, only to a certain degree, as the cause of the toxic process which develops in the intoxicated organism. Fundamentally, this applies to those toxic effects which are associated with a disturbance in the parasympathetic innervation of such organs as the heart, bronchi, gastrointestinal tract. It is impossible to explain completely the effects of organic phosphorus compounds on the central nervous system simply by this effect; the disturbance in the function of the central nervous system is the chief link in the pathology of intoxications by these substances.

Therefore, further investigations are needed for the

clarification of the biochemical mechanism of action of organic phosphorus compounds.

Second Lecture

Pathogenesis of Intoxications by Organic Phosphorus Compounds

The pathogenesis of injuries produced by organic phosphorus compounds is complicated. Some aspects of it are still unclear. The most characteristic disturbances in these intoxications occur in the central nervous system, respiratory organs and circulatory organs.

Central Nervous System

The cerebral cortex is very sensitive to the effect of organic phosphorus compounds and reacts to them even in those cases where the signs of injury of other organs and systems are have not yet manifested themselves. Thus, under the influence of even small doses which do not notably affect the blood pressure level or nature of respiration, the excitation processes of the cerebral cortex are increased, which is evidenced by changes in the chronaxie of the cortical area, the electrical activity of the brain and the conditioned-reflex activity of the body. In severe intoxications there is also first noted an increase in the excitability which is manifested in the form of motor excitation, which occurs either in response to external influences or spontaneously; there is a feeling of anxiety. The

increase in excitability is, after a certain time (usually quite quickly), replaced by a depression in the cortical functions: adynamia, general listlessness, clouding of consciousness and then a complete loss of consciousness develop.

Therefore, a biphasic course is observed ~~after injury~~ in the central nervous system after injury with organic phosphorus compounds.

It would be an error, however, to believe that the central nervous system reaction to the effect of organic phosphorus compounds is limited simply to disturbances in the cerebral cortical functions. Experimental investigations performed on decerebrate animals make it possible to state that in intoxication by these substances other portions of the central nervous system are also involved. In such animals, following the administration of the toxin, characteristic signs of intoxication occur in the form of disturbances in the circulation and respiration as well as convulsions which stop only after the destruction of the spinal cord. Disturbances of respiration, changes in the blood pressure level as well as a disorder in the functions of the vagus nerve center are the result of injury to the medulla.

Therefore, all parts of the central nervous system are involved in the pathological process from intoxication by organic phosphorus compounds, but this is not manifested simultaneously and is expressed to different degrees at various stages. The signs of cortical excitation occur rapidly and are maintained for quite a long time. Only brief and insignificant signs of excitation are characteristic of the

medulla (at least for some of its centers), and these are rapidly transformed to a depression. The cerebral cortical function is impaired from the effect of very small quantities of the toxin. The various centers of the medulla are quite sensitive also. The spinal cord, on the other hand, is more resistant; a disturbance in its functions usually occurs later and from the effect of large doses of the toxin. Since in different organisms the degree and nature of disturbance in the functions of various portions of the central nervous system are different, the sequence of involvement of them in the pathological process is also different. As a result of this, in intoxication by organic phosphorus compounds there may be a great number of variants in the clinical manifestations.

The data presented permit us to draw the following conclusions:

1) All parts of the central nervous system are involved in the pathological process after injury of the body by organic phosphorus compounds.

2) The central nervous system reacts first to organic phosphorus compounds by excitation, which then passes into depression.

3) After injury to the body by organic phosphorus compounds the rate of involvement of various parts of the central nervous system and the intensity of disturbance in its functions vary. The cerebral cortex is most sensitive.

The mechanism of occurrence of functional disorders of the central nervous system after injury by organic phosphorus compounds has not been conclusively studied. The fact is indubitable that changes in the central nervous system functions depend both on direct contact with the toxin and on the occurrence of pathological impulses which come from the periphery to the central nervous system, particularly, from disturbances in its normal interrelationships with the external and internal milieux of the body.

Therefore, in the study of the pathogenesis of intoxications by organic phosphorus compounds an important place is occupied by disorder of the central nervous system functions, which is evidenced by the occurrence of convulsive attacks. It has been shown by experiments with decerebration that convulsions which occur from the injury depend to a considerable degree on the effect of the toxin on the spinal cord, proof of which is the prompt cessation of them after destruction of the spinal cord.

Therefore, in these injuries the convulsions have a central rather than peripheral origin, and the occurrence of them is associated with the effect of the toxin on the number of parts of the central nervous system, from the motor area of the cerebral cortex to the spinal cord. Along with changes in the cerebral cortical functions the intoxication produces considerable disturbances in the functions of other central nervous system sections also. Thus, disorders of respiration are associated with the effect of the toxin

on the respiratory center, and the disorders of circulation are associated with a disturbance of the vasomotor center. At the same time, disturbances in the vasomotor center may depend on the pathological changes in the respiratory center.

All this speaks for the tremendous part of the central nervous system in pathology of intoxication by organic phosphorus compounds. This central nervous system reaction is associated, on the one hand, with a direct effect of the toxin on the brain tissue; on the other hand, with a disturbance of the ordinary interactions of the central nervous system with the external and internal milieux. These are the causes of occurrence of a number of functional changes in the central nervous system which are expressed as various signs of intoxication. The nature of these changes is accounted for, in large measure, by the protective role of the cerebral cortex.

Vegetative Nervous System

Intoxication by organic phosphorus compounds produces a number of disorders in the activity of smooth-muscle organs and glands (eyes, bronchi, intestine, salivary glands, etc.), which gives us the grounds for speaking of disturbances in the functions of the vegetative nervous system (parasympathetic and sympathetic), particularly the parasympathetic.

Among these disorders are the following: constriction of the pupil (miosis), spasm of accommodation, macropsia, which is manifested as a distortion of subjective perception of the eyelashes and

other objects. The signs of intoxication mentioned are brought about by injury to the oculomotor nerve, which is part of the parasympathetic system. The bronchospasm and signs of bradycardia, which are observed during the intoxication, also speak for involvement of the parasympathetic nervous system in the pathological process. The increase in the secretion of the salivary and bronchial glands as well as spasm of the intestine speak for the same thing. The close connection in the development of the signs mentioned above with injuries to the parasympathetic nervous system is confirmed by experiments with atropine. The use of this alkaloid, which paralyzes the transmission of impulses from the post-ganglionic parasympathetic fibers to cells of efferent organs, eliminates the signs of disturbance in the functions of the smooth-muscle organs, heart and glands. It has been determined also that atropine in isolated organs prevents the development or eliminates already existing functional disturbances. This injury to the parasympathetic nervous system is associated with the effect of the toxin both on the central and the peripheral nervous systems.

In the clarification of the mechanism of the toxic effect of organic phosphorus compounds on the body it is necessary to take into consideration the effect of the toxin on the sympathetic nervous system. Functional changes of the vegetative nervous system have to be tied in with disturbances occurring in the central nervous system. The data presented show that intoxication with organic phosphorus

compounds occurs with signs of disturbances in the functions of both portions of the vegetative nervous system, but with predominant involvement of the parasympathetic portion.

The mechanism of functional disturbances in the vegetative nervous system from intoxication with organic phosphorus compounds is associated with a disturbnace in the chemical transmission of nerve impulses, that is, basically with deep-seated changes in the acetylcholine metabolism. Primarily, this is manifested in a disorder of function of the parasympathetic nervous system, which is most intimately connected with acetylcholine as a mediator. The mechanism of injury to the sympathetic nervous system, the function of which, as is well known, is regulated by two mediators -- acetylcholine and sympathin -- is somewhat more complicated. However, even here the disorders may also depend on disturbances in the acetylcholine metabolism.

Therefore, the data presented indicate the great complexity of the mechanism of disturbances in the functions of the vegetative nervous system from intoxication by organic phosphorus compounds.

Disturbances in the Motor Nerves

In the case of injuries by organic phosphorus compounds characteristic changes in the functions of the transversely-striated musculature occur which are expressed in convulsive contractions of muscles (clonic or tonic), fibrillary twitchings of muscle fibers, weakness or paresis. The occurrence of convulsions is connected with a disorder in the central nervous system functions, because after a

disturbance in the integrity of the spinal cord the convulsive contractions promptly stop. The occurrence of fibrillary twitchings in the muscles depends on an increase in the excitability of the nerve-muscle synapse. Hereby, the impulses proceeding from the central nervous system, without interfering without the functions, lead to an increase in the reactions of the striated musculature.

Respiratory Disturbances

After intoxication by organic phosphorus compounds considerable disorders occur in the respiration, the degree of expression of which varies and depends on a number of circumstances including on the route of entry of the toxin into the body. After inhalation intoxication respiratory disturbances are expressed to a greater degree than after percutaneous application or administration of the toxin through the digestive tract. However, this applies only to mild and moderate injuries. In the case of a severe degree of intoxication a marked depression of respiration occurs regardless of the route of entry of the toxin. Respiratory disorders, by interfering with the conditions of arterialization of the blood, lead to disorders in its gas content, as a result of which a considerable hypoxemia occurs, which in its turn cannot help but affect the activity of the organism and primarily the functions of the central nervous system. In the study of the mechanism of these disorders it has been determined that the main cause of their occurrence are spasms in the bronchial musculature and a disturbance in the functions of the respiratory

center rather than convulsions. Clinical observations have shown that changes in the respiratory center functions occur biphasically: at first, a brief excitation is noted which is then replaced by a prolonged depression. With mild intoxication, an increase in the respiratory rate is observed in the initial stage which is then replaced by a slowing and a decrease in the amplitude of the respiratory movements. Subsequently, the respiration becomes normal and of the usual type. With a severe degree of injury, as a result of disturbance in the functions of the respiratory center, the respiration first increases in frequency and becomes deeper but it soon after becomes superficial and irregular with pauses and, finally, stops completely. The respiratory center is very sensitive to the effect of organic phosphorus compounds.

Therefore, respiratory disturbances during intoxications represent a most important pathological process which occurs as the result of the effect of the toxin on the central and ~~nervous~~ peripheral nervous systems. In a practical connection, ~~it is~~ the reversibility of the disturbances in the respiratory center functions ~~are~~ is very important. Even in cases of serious intoxications, with the prolonged use of artificial respiration (two to three hours), it is not uncommonly possible to restore independent respiration.

Circulatory Disorders

In the pathology of intoxications by organic phosphorus compounds considerable importance is ascribed to a disturbance in the

circulation, along with the respiratory disorder (the fluctuations in the level of the arterial and venous pressures, change in the strength and frequency of the cardiac contractions). In cases of severe intoxications particularly considerable changes in the blood pressure are noted. In the initial stage, its level increased to varying degrees; an increase in the amplitude of the pulse pressure is characteristic; here, the diastolic pressure increases slightly, whereas the systolic increases considerably. The nature of the subsequent changes depends on the severity of intoxication. In the mild forms of intoxication the blood pressure usually levels off gradually; in the more severe forms, it decreases progressively and falls to zero.

The causes of the blood pressure changes in intoxications by organic phosphorus compounds has not been clarified conclusively. Possibly, specifically the different conditions of blood vessels of different areas during the intoxication are one of the determining causes of the difference in the venous pressure levels. Here, a major part is played by changes in the vascular tone, which is associated with injury to the vasomotor center of the medulla.

Impulses coming from the periphery to the central nervous system have less of an influence on changes in the blood pressure level. In this respect, data concerning the respiratory center are entirely applicable to the vasomotor center. It should be kept in mind that the functional condition of the vasomotor center in intoxication by organic phosphorus compounds depends a great deal on the tone

of the respiratory center, the degree of asphyxia, disorders in the blood circulation and cardiac activity.

In the initial phase of intoxication a slowing of the cardiac rate is observed. In the mild forms of intoxication the strength of cardiac contractions usually is unchanged, but the so-called "vagus" pulse with a high pulse pressure amplitude appears.

A slowing of the rhythm of cardiac activity is associated with a slowing in the circulation, proof of which is constituted by experiments with atropine, which, by eliminating the slowing in the cardiac activity, leads to the restoration of the normal circulation time.

Disturbance in the cardiac functions is associated with the direct effect of the toxin on the heart. Here, impulses coming from the central nervous system also exert an influence. The organic phosphorus compounds influence not only the myocardium but also the vegetative nervous system, in connection with which the cardiac rhythm is changed and conduction is impaired. These substances also cause a constriction of the coronary blood vessels, whereby the cardiac muscle circulation is impaired and therefore also the conditions for cardiac activity. Spasm of the bronchial musculature, which occurs during injury by the organic phosphorus compounds, can also lead to a constriction of the blood vessels in the lesser circulation with a subsequent increase in the pressure in the veins and difficulty in cardiac function. The possibility has not been ruled out that overfilling of the

venous system leads to the occurrence of corresponding nerve impulses which have a harmful influence not only on the work of the heart but also on the function of the central nervous system.

The data presented show that after intoxications with organic phosphorus compounds the circulatory disorders and the disorders in cardiac activity have a very complicated pathogenesis. At the same time, along with the respiratory disorders, they are the most markedly expressed disturbances in the functions of the body from injuries by these substances. In many cases, injuries to the circulatory and respiratory systems are so considerable that they determine the severity and outcome of the intoxication.

The Clinical Aspects of Injury by Organic Phosphorus Compounds

The clinical picture of intoxication by organic phosphorus compounds depends not only on the quantity of them and the individual reaction of the body, but, in large measure, are brought about also by the routes of entrance of the toxin into the body. The main data on the study of the clinical picture of the intoxication by these substances have been obtained under experimental conditions on animals of various species. In the foreign literature considerable clinical material has been published devoted to the course of intoxications with various representatives of the organic phosphorus compounds (diisopropylfluorophosphate, tetraethylpyrophosphate, parathion and others). The similarity of the toxicological dynamics of the various organic phosphorus compounds makes it possible to use these data in

the description of the clinical picture of the intoxications.

Inhalation Forms of Intoxications

The clinical signs in inhalation forms of intoxication by organic phosphorus compounds depend on the time that one is in the intoxicated atmosphere, the concentration of the poison in the inhaled air, as well as on the frequency and depth of respiration during one's stay in the contaminated atmosphere. Three periods can be noted in the clinical picture: a period of restlessness, a convulsive period and a paralytic period. According to the data of Grob, Krop and Loomis, the first signs of intoxication with organic phosphorus compounds are visual disorders: a constriction of the pupils, congestion of the conjunctivae, lacrimation, foggy vision, pains in the area of the eyes. Soon after, restlessness appears, headache, dizziness, apathy, and musculature weakness. A special place in the symptom-complex of intoxication is occupied by respiratory disorders. Cough appears with copious sputum, labored respiration (particularly in the expiratory phase). Respiration becomes superficial and rapid. Afterwards, a picture develops of bronchospasm (Krop, Kunkel, Heymans, Pochet, Houtte). The spasm of the bronchial musculature is associated with a marked increase in the secretion of bronchial glands, which leads to a profuse accumulation of fluid throughout the respiratory tract, by the same token aggravating the serious picture of labored respiration as a result of bronchospasm. As a result of this, asphyxia develops. Vomiting movements not uncommonly accompany the respiratory

disorders, and sometimes there is vomiting and a profuse excretion of a viscid saliva. Ten to 15 minutes after the intoxication a stormy convulsive attack of tonic and clonic nature usually occurs, which lasts approximately three to five minutes and is associated with involuntary defecation and urination. Then, the first convulsive attack subsides. There is no reaction to pain stimulation; the corneal reflexes are intact. The convulsive attacks are repeated at various intervals, measured in minutes, but become shorter and are not so vigorous as at first. In the intervals between the convulsive attacks there is complete prostration, the respiration is markedly weakened and superficial. Marked salivation lasts throughout. Gradually, the convulsive attacks become less frequent, and a comatose condition is observed. Death occurs from stoppage of respiration, and after one or two minutes the cardiac contractions also stop. Individual variations are noted in the duration of the entire cycle of intoxication which lasts from several minutes to two to three hours. Only a small part of those intoxicated die at the end of the first day. In some cases the course of intoxication is characterized by an almost complete absence of convulsions. Death occurs during the first few minutes after the intoxication with signs of asphyxia as a result of respiratory disorders.

Among the important pathological signs of injury by organic phosphorus compounds mention should be made of circulatory disorders which are particularly closely associated with changes in the

respiratory functions. One of the early signs of disturbance in the circulation is a change in the cardiac activity which is confirmed by a deformation of the electrocardiogram. Most characteristic here is a lengthening of the P-R interval and of the QRS as well as a complete block with disappearance of the P wave (Krop and Kunkel).

The reduction in the work of the heart is expressed also in a reduction in the arteriovenous difference, which is observed, according to Holmstedt's data, before the occurrence of changes in the blood pressure. At the beginning of the intoxication there is sometimes noted an increase in the blood pressure (Krop and Kunkel, Grob, Garlich and Harwey); sometimes, it is decreased. The venous pressure is usually decreased. The pulse is soft, easily compressible, and increased in rate.

In some cases the body temperature is increased to 38-41°C; in others, the temperature changes are not found (Grob, Garlich, Merrill, and Freimuth).

The changes in the blood, according to the data of Grob, Garlich and Harwey, amount to a slight increase in the leucocyte count. In the differential leucocyte count a moderate increase is noted in the polymorphonuclear cells. The content of red blood cells, hemoglobin and the sedimentation rate do not undergo any essential changes.

If the patients live through the acute period of intoxication the convulsions subside, and consciousness is restored. Despite the

apparent improvement, death can occur even in the late period: the blood pressure suddenly falls, the pulse becomes thready; the respiration becomes rapid and superficial, and a pronounced cyanosis appears. Death occurs with increasing signs of vascular insufficiency. In some cases the signs of vascular collapse become the predominant ~~sign~~ symptom from the very beginning of the intoxication, and the respiratory disturbances and convulsions are not very prominent.

As an illustration of what has been stated a case is being presented below of intoxication with one of the group of alkyl phosphates, described by Grob.

A man 35 years of age was working with alkyl phosphates in his work clothes (a carbon filter respirator, protective goggles, rubber gloves, high rubber boots, a rubber apron and a protective mantle, which did not completely cover his arms and his back). Suddenly he felt nausea and calls to defecation. These phenomena continued for 30 minutes, and then a profuse perspiration, dizziness, headache, a blackening before the eyes, restlessness, musculature twitchings of the tongue and eye lids, and general musculature weakness were superimposed. He was put in the hospital two hours after the occurrence of the initial symptoms.

The examination data showed the following: he was well developed and he walked spontaneously. He was excited, restless, had twitchings; however, he was well oriented. A profuse perspiration was observed with marked salivation. The speech was slightly difficult;

there was repetition of the last word and syllable. The pupils were constricted (punctate); it was impossible to examine the optic fundus. The respiration was 16 per minute; there were no changes in the lungs. The heart was normal on percussion and auscultation. The pulse was 92 a minute. The blood pressure was 152/126 millimeters of mercury (the blood pressure before the intoxication was 100/70). There was a fibrillation of the muscles of the tongue and lids and irregular jerky movements of the eyeballs. Soon, the muscle fibrillations became generalized, and a very severe muscular weakness developed. The tendon reflexes were normal; there were no pathological reflexes.

Forty minutes after hospitalization the patient gradually began to go into a comatose state. The tendon and the pain reflexes disappeared. Attacks of convulsions developed. In the intervals between the convulsive attacks there was Cheyne-Stokes respiration (which was stopped by inhalation of a mixture of five percent CO_2 and 95 percent O_2). There was no definite picture of bronchospasm. The lungs were normal. The blood pressure was 186/100. There was no noticeable hypoxemia. There were frequent calls to defecation and urination; the stool was watery. The vomitus was liquid with an odor. One pupil dilated slowly after the repeated administration of atropine (one percent solution, one drop every 15 minutes). After a half hour the pupils again constricted.

The treatment was atropine sulfate, 0.6 milligram

intramuscularly in one hour led to a reduction in perspiration, salivation and bronchial secretion. The drip administration of physiological solution and glucose was given. In the first attack of convulsions curare eliminated the fibrillations, and made the convulsive attacks milder but did not prevent the occurrence of the next attack.

For four hours the patient was in a comatose state; the reflexes were absent. After seven hours the pain and tendon reflexes began to be restored. The pupils dilated somewhat, and a slight reaction to light appeared. The blood pressure gradually decreased to 150/80. After one hour, consciousness returned; the patient noticed that his vision was clouded and he saw objects as though in a fog. For the next two hours the patient's condition improved; he answered questions more rapidly and spoke better. However, in the tenth hour after the occurrence of the first symptoms of intoxication respiration became superficial, frequent, and labored; the pulse could not be felt. After ten hours and 15 minutes, the patient died.

Wilhelmi and Domenjoz also have described cases of intoxication with alkyl phosphate, whereby in the beginning the following were noted: perspiration, lacrimation, salivation, nausea, vomiting, diarrhea, intestinal colic, dyspnea, bronchospasm, marked miosis, a disorder of accommodation, a reduction in the body temperature; then, edema of the lungs developed and there were muscle fibrillations and convulsions. In the serious cases, ataxia, tremor, dizziness,

vertical nystagmus, sleepiness, weakness, confusion, retarded speech, and a comatose state were noted. Sometimes, in the beginning an increased blood pressure was noted with a marked leucocytosis. In the late stages of intoxication the following were observed: cyanosis, decrease in blood pressure, dyspnea and a disturbance in cardiac activity. Death from severe intoxication occurred in 14 hours. In those cases where the patients recovered the signs of intoxication disappeared after 12-24 hours.

A number of authors (Grob, Garlich and Harwey) distinguish muscarinic and nicotinic effects among the various signs of intoxication with organic phosphorus compounds as well as symptoms connected with the effect of these toxins on the central nervous system.

Muscarinic Symptoms. The first symptoms of this group are anorexia and nausea, which increased after smoking and frequently were accompanied by vomiting, spasmodic pains in the abdomen and salivation.

With the increase in the signs of intoxication diarrhea, tenesmus, involuntary urination and defecation are possible. Among the symptoms of this group mention should be made of constriction of the pupils, increase in blood pressure as well as disturbances observed in the process of respiration (excessive bronchial secretion, bronchospasm, and pulmonary edema).

Nicotinic Symptoms. In this group of toxic phenomena mention should be made of twitching of the eye muscles and tongue, which occurs immediately after the nausea and vomiting and which are early signs of intoxication. In the severe cases twitchings of the muscles of the face and neck are observed which change into convulsive attacks. Sometimes, there are no convulsions, and signs of increasing weakness and atony are observed.

Central Nervous System Symptoms. The earliest symptoms are the following: dizziness, restlessness, a feeling of anxiety. These symptoms occur shortly after the anorexia and nausea. Subsequently, headache and insomnia are observed. In the more severe cases of intoxication the following develop: ataxia, tremor, disorientation for the surroundings, changes in speech (difficulties in formation of words, repetition of the last syllables). These symptoms frequently precede the comatose condition with complete loss of all reflexes. During coma Cheyne-Stokes respiration, convulsions and a marked constriction of the pupils are noted.

Therefore, in intoxication with organic phosphorus compounds signs of involvement of the central nervous system are prominent, which is expressed in the development of convulsive and then paralytic phenomena. This also makes it possible to categorize tabun, sarine

and other organic phosphorus compounds among the group of nerve toxins (Grob, Krop and Loomis, Kondritzer, Elam, Clements and others). Here, (as has been mentioned by Jaques, Bein and Meier) in intoxications with organic phosphorus compounds involvement occurs not only of the central nervous system (brain and spinal cord) but also of its peripheral portion. Excitation of the central and peripheral portions of the somatic and vegetative nervous systems which are observed are replaced by paralysis of them.

It should be noted that in the inhalation form of intoxication toxic phenomena (restlessness, feeling of anxiety, feeling of compression in the chest, disturbances of vision) can occur at the time of inhalation of the toxin. Despite the considerable similarity in the nature of the intoxication and its dynamics, the clinical course of intoxication with organic phosphorus compounds is induced to a certain degree by the method of application of the toxin (percutaneously, orally, etc.).

Intoxications Associated With Contact of the Toxin With the Skin

When organic phosphorus compounds come into contact with the skin signs of irritation of the skin are absent (Krop and Loomis, Deichman, Puglise, Cossida); the toxin is usually absorbed into the body and produces intoxication. With the skin-absorptive effect of

these compounds the first signs of intoxication are found after several minutes in the majority of cases, although they may developed even after one or two hours. The first signs of intoxication, regardless of the time of their occurrence, are, according to the data of duBois and coworkers, Deichman, Puglise and Cossida and others, restlessness, uncoordinated movements, lacrimation, a lessening of muscle tone, involuntary urination and defecation. Afterwards, fibrillary twitchings of various muscle groups are observed. In the more severe cases of intoxication convulsive twitchings of the muscles of the trunk are superimposed on these signs, which terminate in clonic or tonic convulsions. It should be noted that in this form of intoxication (absorption of organic phosphorus compounds from the surface of the skin) changes in the eyes (constriction of the pupils and others) may be absent (Deichman and others). As a result of absorption through the skin of large quantities of the toxin a serious intoxication develops the first sign of which is restlessness. Afterwards, the following are noted: dyspnea and increased salivation; the respiration becomes gradually slower and irregular; the pulse increases in frequency and sometimes an arrhythmia. After several minutes fibrillary twitchings appear in the muscles of the trunk; later, convulsive contractions of the muscles of the extremities.

Soon after, a tremor and clonic and tonic convulsions appear which usually change into convulsive contractions of the entire body. During the attack of convulsions the corneal reflexes disappear, involuntary urination and defecation are observed. The duration of the course of intoxication varies: from 30 minutes to several hours. Death occurs with signs of marked depression of the central nervous system functions, absence of reflexes, a slow irregular respiration and disturbance in circulation. It should be noted also that the skin-absorptive intoxications occur, as a rule, without the development of miosis, with less pronounced respiratory disorders and longer latent periods than in the inhalation form of intoxication.

Oral Forms of Intoxications

The good solubility of organic phosphorus compounds in water and organic solvents and their adequate stability make possible their contamination of water bodies, storehouses, etc. Therefore, they may constitute a threat of entrance into the body in water and food. It has been determined by experimental investigations that organic phosphorus compounds are less toxic after entering the stomach than after some other forms of application (inhalation, contact with the skin). At the same time, the toxicity of many of them is, nevertheless, considerable.

The clinical aspects of oral intoxications are heterogeneous. In the mild forms, the signs which are most striking are in the gastrointestinal tract, whereas in the severe forms, disturbances in the function of the central nervous system predominate.

In the mild forms of intoxications, usually after the entrance of the toxin into the stomach in the water or in the food, a latent period is observed the duration of which is very variable (from five to 30 minutes); this apparently depends on the degree of filling of the stomach, the type of food products with which the toxin enters and the rate of absorption of the toxin by the gastric mucosa. At the end of the latent period the following occur: deepened respiration, salivation and vomiting movements. The vomitus consists of water and food which are in the stomach; subsequently, the quantity of it decreases; in the vomitus there is mucus with an admixture of bile and sometimes blood. After 20-30 minutes a profuse diarrhea is superimposed, which lasts for hours. Usually, on the next day vomiting and diarrhea are not found. The general condition is characterized by a depression and listlessness, which gradually decrease and disappear after two to three days.

Intoxication of moderate severity is characterized by the same symptoms but more intense. The vomiting is of a more stubborn

and prolonged nature; the diarrhea continues for several days. The general condition remains depressed for two to four days; there is no appetite or it is markedly decreased. Recovery occurs slowly. In some cases the general condition begins to deteriorate progressively, and a marked depression of the central nervous system occurs which leads to death. In other cases, beginning with the third-fourth day the general condition improves, the appetite returns, and the stools become normal; on the seventh-12th day the patient recovers.

The symptoms of the severe intoxications in the initial period are characterized by vomiting, diarrhea and increased reactivity. Simultaneously, there is an increase in salivation and dyspnea appears. After 10-20 minutes fibrillary twitchings appear in various muscle groups, which change into a general tremor. Shortly afterwards, the following are found: adynamia, a disturbance in the coordination of movement and muscle weakness. Afterwards, an attack of clonic convulsions develops which changes into tonic convulsions. Thereby the corneal reflexes are extinguished, the pupils dilate, the respiration is impaired, and marked cyanosis is noted. Death occurs against the background of a progressive weakening of respiration and cardiac activity.

Third Lecture

Clinical Forms of Intoxication With Organic Phosphorus Compounds

According to the severity of the course the following clinical forms of intoxications with organic phosphorus compounds are distinguished: mild, severe and chronic. The mild forms of intoxication occur a certain time (from several minutes to one to two hours) after contact of the patient with the toxin. The first signs of involvement are in the eyes -- miosis, and spasm of accommodation. Less often, lacrimation is noted. Seeing objects in the dark becomes quite difficult. The pupils are constricted down to the size of a pinhead and react slightly to light (in individual cases this reaction is completely absent). The conjunctiva becomes congested and sometimes edematous. Along with the feeling of discomfort and slight pain in the eyes, painful sensations occur in the temples and in the area of the frontal sinuses. In the persons affected there are sensations of dyspnea, and the respiration becomes labored; an increased salivation, nausea and vomiting are noted. The respiration becomes strained; there

are râles, and sometimes aphonia occurs. The pulse is slowed, and in some cases it is labile. This condition lasts for several hours. The pathological signs gradually lessen, whereby the first to subside is the sensation of choking. The further course of the intoxication is of a wave-form nature: an alternation of remissions and considerable deteriorations in the general condition. Recovery occurs after one or two days; thereby the signs of miosis are observed up to two or three days.

In the more severe cases the initial signs of intoxication are similar to the signs in the mild form. Subsequently, the signs of intoxication increase. The miosis reaches its maximum degree (the pupils are constricted down to the size of a pinhead and do not react to light); there is a marked spasm of accommodation; the vision is limited simply to light perception. Respiration becomes markedly labored, superficial, of increased frequency, and cyanosis appears with increased salivation; in individual cases there is persistent vomiting. The pulse slows (50-60 beats a minute). Brief attacks of tonic convulsions are observed. In the urine, blood and spinal fluid there are no pathological changes. Subjectively, the intoxication occurs in a torturesome manner: there is a general excitation, a feeling of anxiety, severe headache, melancholy and general weakness.

The course of these forms of intoxication is more prolonged. The intensity of the symptoms lessens after 24 hours; however, miosis and bronchospasm remain for several days. It should be noted that these forms of intoxication occur without any deep-seated disturbances in the functions of the respiratory center and without any considerable disorders of the circulation. The persons afflicted should be treated under conditions of complete rest, because physical exertion causes a marked deterioration in their general condition. Complete recovery occurs after five to ten days.

The clinical course of the severe forms of intoxications is varied. In severe cases, considerable central nervous system disorders are most characteristic along with disturbances in the functions of various organs and systems. Here, a latent period may be observed the duration of which usually does not exceed 20-30 minutes. In intoxication with large doses a latent period may be absent. The occurrence and degree of development of the signs of intoxication depend a great deal on the route of entry of the toxin. The inhalation of air containing vapors of organic phosphorus compounds produces marked choking and a considerable constriction of the pupils. After absorption through the skin the chokihg is less pronounced and there may be no miosis.

In the severe forms of intoxication the intensity of the symptoms which appear after the latent period (miosis, bronchospasm and others) increases progressively. Excitation and a feeling of anxiety and general weakness are superimposed on them. Consciousness is gradually clouded. Convulsive twitchings of various muscle groups appear and then twitchings of the entire body. The convulsions have the nature of paroxysms. In the intervals between the paroxysms the unconscious state may be replaced by a considerable excitation and motor restlessness. During the convulsive attacks as well as in the period between convulsions various respiratory disorders occur and cyanosis appears. Nucus is excreted from the mouth and nose. Frequently, vomiting is observed. The blood pressure is decreased; the pulse becomes slow, arrhythmical and of poor quality, sometimes thready. In the most severe cases the convulsive attacks are accompanied by progressive weakening of respiration with a subsequent stoppage of it.

A marked deterioration of the general condition in those intoxicated may occur even during the period of relatively satisfactory condition. Therefore, the persons intoxicated with organic phosphorus compounds require particularly careful observation. The intoxications without any marked depression of respiration or

disorders in the vascular system have a more favorable course.

No pathological changes are observed in the urine or spinal fluid. In the blood there is a leucocytosis and shift to the left in the differential white blood count. The signs of intoxication are preserved for several days, and then they gradually disappear.

After the effect of very large doses the severe cases may have a fulminant course. In these cases, the latent period is very short. Convulsions develop rapidly, following one another without any intervals.

The chronic intoxication with organic phosphorus compounds may be produced by the repeated effect of small doses of the toxin. Chronic forms do not have any specific clinical picture. According to Barnes, this form of intoxication is characterized by a delayed and sluggish course of the acute syndrome.

Therefore, the principal manifestations of intoxication with organic phosphorus compounds indicate the involvement primarily of the central nervous system in the pathological process. In mild cases the disturbances amount to a disorder in the visual organs and in respiration. Intoxications of moderate severity are characterized by pronounced disorders of the central nervous system functions

accompanied by torturesome subjective sensations. In the severe intoxications the clinical course and outcome of the intoxications are determined by the degree of disturbances in the central nervous system function. The direct cause of death is depression of the respiratory center with subsequent paralysis of it.

Late Consequences

The prognosis with respect to recovery in persons intoxicated with organic phosphorus compounds depends a great deal on the severity of the intoxication. In cases of mild forms of intoxication the prognosis is usually favorable, and recovery, in the absence of complications, occurs during the first two weeks. In connection with the prognosis, severe injuries, particularly in those cases where marked depression of the respiration and cardiovascular activity develop, are dangerous.

Intoxications which end in recovery, however, do not always disappear without trace. In such persons the following are observed for a long time (many months) after recovery: rapid fatigability, marked headaches, general weakness, a staggering gait; a disturbed central nervous system function remains in the form of increased irritability, tendency toward insomnia, rapid exhaustability of the nervous system, instability of the vegetative nervous system (Reinl).

A decrease in the blood cholinesterase activity is maintained for a very long time. It should be noted that the relationship between the severity of intoxication and the degree of depression of cholinesterase activity in the blood is not always observed in the those afflicted. For a long period of time in those who have suffered intoxication a tendency remains toward regularly appearing paroxysms of bronchospasm and pneumonia.

Differential Diagnosis

In making the diagnosis it is necessary to take into consideration the routes of entrance of the toxin into the body. The inhalation form of intoxication is the easiest type of human injury with organic phosphorus compounds to diagnose; here, very early and characteristic differential-diagnostic signs are observed in the eyes: constriction of the pupil to the size of a pinhead, spasm of accommodation, manifested in a disturbance in perception of distance and in the sizes of objects which appear to be increased (macropsia). Here, congestion and a certain edema of the mucosae of the eyes are possible. Respiration is disturbed; it becomes very much increased in frequency and irregular; paroxysms of bronchospasm appear. In cases of severe intoxication an increased salivation, increase in the muscle tone and fibrillary twitchings and convulsions develop.

After contact of the liquid substance with the skin, if the person affected has been in a gas mask, the signs in the eyes as well as bronchospasm may be absent or may be slight.

After intoxication through the gastrointestinal tract (use of contaminated food and water) a stubborn vomiting and diarrhea are characteristic; there is a rapid development of signs in the nervous system.

In all forms of intoxication of signs of excitation of the central nervous system in the form of restlessness, convulsions, etc. develop in moderate and severe cases.

It should be kept in mind in the differential diagnosis of injury by organic phosphorus compounds that they do not possess a cutaneous effect. Based on this, there are no particular difficulties in diagnosing them differentially from lesions produced by vesicants, wherein the inflammatory-necrotic processes in the skin and mucous membranes are pronounced, and there are no characteristic miosis and bronchospasm, as is seen with the organic phosphorus compounds. Sometimes, there may be a difficulty in the differential diagnosis from lesions produced by asphyxiants. However, the development of signs of toxic pulmonary edema (early hemoconcentration, cough, profuse copious sputum, etc.) without signs of bronchospasm

orspasm of accommodation are characteristic of the latter. The signs of injury to the eyes are limited usually to lacrimation and a mild conjunctivitis after the effect of asphyxiants. In cases of injury with lacrimatory and particularly irritant war gases, a profuse secretion is observed from the mucosae of h the upper respiratory tract with marked lacrimation. All this is accompanied by a very severe pathology and signs of irritation of the mucous membranes (severe hyperemia, edema).

Intoxications with hydrogen cyanide offer the greatest difficulty for the differential diagnosis of organic phosphorus compound injuries. However, in the former case there are absolutely no signs of eye involvements; the pupils are unchanged or even somewhat dilated, and the odor of bitter almonds is perceived in the exhaled air; the mucous membranes are pink. Hereby, the convulsions are of a clonic-tonic nature and disappear rapidly.

After intoxication with carbon monoxide a dilatation of the cutaneous capillaries is observed (on the face, thighs, etc.). The blood is of a bright aloe color, contains carboxyhemoglobin. The depression of the nervous system is more pronounced. There are no particular difficulties in distinguishing organic phosphorus compound intoxication from intoxications produced by arsine (prolonged latent

period, hemolysis, and lesions in the liver and kidneys).

In cases of moderate and severe injuries the most reliable and specific differential diagnostic feature in intoxication with organic phosphorus compounds is a reduction in the cholinesterase activity in the blood. For the purpose of determining the diagnosis in all forms of intoxication it is essential to make a careful comparison of clinical signs of intoxication with the data of the history and the conditions under which the intoxication occurred.

Pathology

It is well known that the pathological changes in intoxication with toxic substances, among which are the organic phosphorus compounds, are usually not so distinct and are much less varied than, for example, in the case of injury by various representatives of the group of vesicants or asphyxiants. This fact creates certain difficulties for the physician or pathologist, particularly in those cases where determining the pathological changes pursues the aim of diagnosis. This is explained, on the one hand, by the distinctive nature of the effect of organic phosphorus compounds on the body (chiefly the effect on the nervous system and blood vessels), and, on the other, by the insignificant length of life of those intoxicated after contact with the poison. Naturally, there may

simply be no development of pathological changes here.

Very characteristic of the intoxication with organic phosphorus compounds is the unitypicality of the morphologic picture. Pathological changes in the various representatives of this group of compounds are the same, by and large, and the differential diagnosis between various organic phosphorus compounds should be considered impossible in practice. The method of effect of the toxin on the body, the route of penetration do not produce any noticeable differences either in the pathological picture of the internal organs in those afflicted. The morphological changes in the various species of animals also develop according to an approximately unitypical pattern. From what has been stated above it does not follow, however, that the pathological method cannot contribute anything valuable in solving the problem of the diagnosis of intoxications with these toxins. In the evaluation of the pathological picture in its totality as well as in supplementing the autopsy data with a careful microscopic investigation adequate starting points may be found for a correct postmortem diagnosis of intoxication with organic phosphorus compounds. As is well known, the latter chiefly affect the nervous system (central and vegetative), enzyme systems (particularly, cholinesterase) and also markedly impair the processes of blood circulation.

In the clinical picture of intoxication signs of involvement of the central nervous system (convulsions) and of the parasympathetic nervous system (miosis, bradycardia, salivation, diarrhea) predominate. In connection with this the principal groups of changes, characteristic in general, of all cases of intoxication with these toxins may be distinguished in the pathological picture:

1. Marked early and long maintained rigor mortis.

2. Spastic contraction of the smooth musculature the result of which is the following: a) constriction of the pupils, sometimes unequal, in cases of the direct effect of the toxin on the eyes (inhalation injury), which is maintained for a long time; with large doses of the toxin miosis is sometimes observed also with other methods of entrance of the toxin into the organism; b) spasm of the walls of the medium-sized and small bronchi; c) a spastic beady contraction of the intestine.

3. A disturbance in blood circulation, which is expressed in congestion of internal organs and multiple hemorrhages.

The microscopic examination introduces a number of essential additions to this picture, particularly with respect to changes in the nervous system, which will be given below in the presentation of the morphologic changes by organs and systems. Here, still another

characteristic feature of the pathological changes should be emphasized from intoxication with organic phosphorus compounds, namely, the absence of reactive-inflammatory processes. Specifically this circumstance can explain the unitypicality of changes with various routes of entry of these toxins, because the characteristic features in the reactions of those organs through which the toxin penetrates into the body are erased.

It is essential to discuss in greater detail the pathological changes of various organs on autopsy, supplementing the autopsy picture with the most essential microscopic changes. All this may be represented in the form of the following schema:

Skin. The effect of organic phosphorus compounds on the skin does not produce any noticeable local reaction, unless we take into consideration a slight congestion and a slight edema.

Eyes. Constriction of the pupils after the direct entry of the toxin. The absence of any signs in the ocular tunics is characteristic.

Blood. Dark red in color, thick with clots.

Trachea and Large Bronchi. Moderate congestion of the mucous membrane. Foamy fluid in the lumen.

Lungs. In case of death quickly they are pale and collapse poorly. There is a spastic state of the small and medium-sized bronchi;

mucus is present in the intact lumina. There is congestion, hemorrhages, punctate and in the form of patches. There are no inflammatory changes in the lungs. (Ripper, Derobert, Grob)

Heart. In the cardiac cavity there is thick blood, dark red clots. There are small hemorrhages under the endo-and epicardium. With large doses of the toxin there are streaky hemorrhages in both ventricles. With death after ten or more hours dystrophic changes are found under the microscope in the cardiac muscle in the form of a dust-like fatty degeneration of its fibers (I. T. Yareshko-Brakhnova).

Liver. Congestion; at the late stages, fatty and hydropic degeneration; a large quantity of iron-containing pigment (I. T. Yareshko-Brakhnova, Ye. I. Spynu, N. A. Sazonova, Ripper).

Kidneys. Congestion, hemorrhages under the capsule.

Spleen is anemic; at the late stages, there is an abundance of iron-containing pigment.

Pancreas. Multiple hemorrhages, particularly in the area of the head of the pancreas, are very characteristic.

Stomach. Small hemorrhages into the mucous membrane (Naeve).

Intestine. Congestion of the blood vessels of the mesentery, beady spasm of the wall of the intestine, hemorrhages into the mucous membrane (Naeve).

Nervous System. It has already been stated above that the most pronounced changes are observed in the central and vegetative nervous systems. It is believed that intoxication with organic phosphorus compounds distinctive processes of an alterative-dystrophic nature and vascular disorders develop in the central nervous system in the absence of an inflammatory reaction. At autopsy of the cranium attention is attracted by the marked degree of injection of the capillary network of the brain, the pronounced congestion of the meningeal blood vessels and brain matter. The brain tissue is slightly edematous. In the brain-stem area, subcortical ganglia, cerebellum, and less often in the cortex, small hemorrhages are seen (Spynu, Kaempe, Rower, Derobert).

In the case of very rapid death pathological changes are slight and amount chiefly to signs of acute swelling of the nerve cells tigrolysis, and from time to time vacuolization. However, in cases of death after one hour or later, these changes increase in their intensity and become more heterogeneous. At these periods the most varied dystrophic-necrotic changes may be observed in the nerve cells: chromatolysis, hyperchromatosis of the nuclei, various stages of the so-called "severe sickness" (Yu. S. Kagan, Ye. I. Makovskaya, Siedek, Kipper, and Holmes).

Along with the histopathological changes of ganglion cells in

the brain the vascular disturbances are quite distinct: edema of the cerebral tissue, perivascular and pericellular edema. In the blood vessels themselves sometimes an edematous separation of the blood vessel walls may be encountered with swelling of the endothelial cells, lipoid infiltration. It is impossible to establish any strict rules and regulations in the localization of the changes; however, it is believed, that most frequently involved are the cortex, inter-brain, and cerebellum.

Therefore, the pathological data indicate that chiefly the nervous system and blood vessels are affected, that is, the morphological changes thereby should be characterized as neurovascular. It should be emphasized that vascular insufficiency can change into a chronic condition, as a result of which slight influences can lead to late complications (cerebral hemorrhages, etc.).

In conclusion, we should dwell on the possibilities of differential pathological diagnosis. The absence of any reactive-inflammatory processes makes it possible easily to distinguish these changes from what is observed after intoxication with vesicants and asphyxiants. Speaking specifically, a distinction has to be made between organic phosphorus and other representatives of the group of general toxic compounds. In these cases, the characteristic

blood changes from intoxication with hydrogen cyanide and carbon monoxide should always be kept in mind (aloe-colored blood, bright red cadaveric spots); the possibility of making a special chemical (for HCN) and spectroscopic (for CO) investigations; the distinctive nature of the lesion in the brain (symmetrical ischemic necroses in the case of CO poisoning). For intoxication by arsine marked signs of hemolysis are characteristic (jaundice, hemoglobinuria, a distinctive color of the kidneys, enlarged spleen, etc.).

All of the pathological changes mentioned above are not characteristic of intoxication with organic phosphorus compounds. At the same time, after intoxication by the latter, pupillary constriction, a spastic condition of the intestine, large hemorrhages into the pancreas, and on microscopic examination, morphological changes in the brain, should be considered specific to a certain degree.

Prophylaxis, First Aid and Treatment

The specific properties of the organic phosphorus compounds, which consist of an exceptionally high degree of toxicity, an exceptional rapidity of action, and an exceptional power of penetrating not only through the respiratory organs but also through the skin, require timely and correct organization of prophylactic measures.

The protective agents existing on supply (gas masks, mantles

and others) are capable of considerably reducing the danger of intoxication but do not eliminate it completely. When very high concentrations of organic phosphorus compounds are created in the atmosphere the intoxication may occur as the result of inhalation of contaminated air in the time needed to put on a gas mask. The contact of the toxin with the clothes and the absence of the possibility of processing it with the antichemical pack immediately can also lead to the occurrence of intoxication. Finally, the possibility has not been excluded of penetration of the toxin directly into a wound. Therefore, despite the presence of individual protective facilities, the need arises for the use of such prophylactic measures which are capable of considerably increasing the resistance of the body to the effect of the toxin.

Of the considerable number of agents known (atropine, physostigmine and others) which have been proposed for the prophylaxis of intoxications with organic phosphorus compounds, the most active has been shown to be atropine, which is capable of preventing the death of animals intoxicated with organic phosphorus compounds. The mechanism of the prophylactic effect of atropine is brought about by the blocking influence of it on the choline-reactive systems of the body. This makes it possible to recommend atropine and substances similar to

it for practical application.

For the purpose of treating intoxications with organic phosphorus compounds various methods have been proposed recently with the use of agents of antidote, pathogenetic and symptomatic therapy. Such a division is of an arbitrary nature, because in a number of cases it is difficult to p classify one agent or another in only one certain group.

The therapy of intoxications with organic phosphorus compounds is based chiefly on the concepts of the mechanism of the toxic effect of organic phosphorus compounds on cholinesterase and tissue choline-reactive systems, including appropriate elements of the central nervous system. In connection with this, compounds are interesting which are capable in varying degrees of lessening or suppressing the cholinergic effect, namely, substances which possess the capacity of reactivating cholinesterase as well as blocking the choline-reactive biochemical systems which are subjected to the selective effect of the toxin (cholinolytic preparations). The problem of restoration of the activity of cholinesterase at the present time is attracting the progressively greater attention of foreign research workers. Recently, through the works of Walson and his coworkers (Askew, Epstein and Freeman) the possibility has been shown of [illegible]

restoration of the cholinesterase activity which has been depressed by organic phosphorus compounds through the application of hydroxamic acids. The application of these compounds is capable, to a certain degree, of lessening the toxic effect of organic phosphorus compounds. However, it should be noted that among the reactivators of cholinesterase no compounds have yet been found which can be used practically as antidotes. This is brought about by the fact that the given substances in doses close to the therapeutic themselves possess a considerable degree of toxicity; in addition, their therapeutic effect is manifested quite slowly. Nevertheless, as is well known from the foreign literature, searches for active compounds of this kind are continuing and possibly will lead to more encouraging results.

The most effective results have been obtained in connection with the development of methods of treatment based on principles of physiological antagonism. The principal place in these investigations have been occupied by works on the study of therapeutic properties of cholinolytic preparations. According to the data of foreign authors (Heymans and others, Krop and Loomis, Modell and Kropp), of all the cholinolytic agents which have been proposed for the therapy of intoxications with organic phosphorus compounds the best

has been shown to be atropine, which reduces the phenomena of bronchospasm, miosis, salivation and other symptoms. In mild cases of intoxication (inhalation form) characterized by the presence of miosis and signs of a moderate bronchospasm (labored respiration, unpleasant sensations behind the sternum), the use of atropine (either by mouth or subcutaneously in a dose of one milligram) has been shown to be highly effective. It rapidly eliminates the phenomena of bronchospasm and miosis. A good therapeutic effect is obtained thereby not only at the beginning of the intoxication but also several hours after it. When the eyes are affected the use of atropine in the form of eye drops (one to two percent solution) is also effective. It completely eliminates or reduces the phenomena of miosis and causes a dilatation of the pupil. Timely use of atropine in cases of moderate severity of intoxication with organic phosphorus compounds, as a rule, reduces the severity of the intoxication. Thus for example, several minutes after the administration of atropine (subcutaneously, two milligrams), in the presence of signs of marked excitation, the respiration becomes free; the excitation and retrosternal pains decrease; the patient lies peacefully or sleeps. However, a single application of atropine under these conditions is inadequate for complete cure, because after a certain time

the signs of excitation and asphyxia usually recur. A second injection of atropine can again eliminate the signs of the intoxication.

Therefore, with intoxications of moderate severity the subcutaneous injection of atropine eliminates the principal signs of the intoxication. Thereby the therapeutic effect lasts, on the average, for five to seven hours, after which the paroxysms of excitation and asphyxia recur. Therefore, the second application of atropine is necessary. The use of atropine is indicated also in serious cases of intoxication (Grob, Jaques, Bein and Meier). It should be taken into consideration only that the latter exerts a therapeutic effect only for a certain time, after which the general condition again deteriorates, and the convulsions recur. While in intoxications of moderate severity atropine exerts an influence for five to seven hours, in the severe forms this interval of time is considerably shortened and lasts about two hours. In such cases, the repeated and more frequent use of the preparation is indicated; the dosage should be higher than that allowed by the official pharmacopoiea (no less than three milligrams).

Therefore, as a result of utilization of atropine for the mild forms of intoxication a rapid recovery of the afflicted persons

is observed. The use of it for intoxications of moderate severity mitigates the signs of intoxication considerably, and recovery occurs even at the end of the first 24 hours. Finally, in the severe injuries, atropine can save the lives of the afflicted persons, although final recovery drags on for a longer time. The therapeutic effect of atropine with respect to organic phosphorus compounds is,nevertheless of a limited nature. According to the data of foreign authors, it is known that atropine only lessens the convulsive attacks after intoxications with diisopropylfluorophosphate and other organic phosphorus compounds but does not suppress the convulsion completely. It does not exert any influence either on the fibrillary muscular contractions.

Despite the favorable effect, atropine possesses a number of defects (toxicity, inadequate therapeutic effect, etc), and therefore cannot satisfy all the requirements made at present on an antidote for organic phosphorus compounds. In its turn, this has led to a search for new, more active and specific antidotes for the organic phosphorus compounds. At the present time, in addition to the natural cholinolytics (atropine and other alkaloids) synthetic compounds of a similar type may be used in the capacity of such antidotes. In addition, the combination of various preparations of cholinolytic type may be

recommended for purposes of increasing their effectiveness. Thereby, it should be taken into consideration that the therapeutic effect of cholinolytics depends on the time of administration of them after intoxication. The earlier application of them assures a more favorable effect.

As has been stated above, various organs and systems are involved in the pathological process in the case of intoxication by organic phosphorus compounds; therefore, treatment of such intoxications should be based on the use not only of preparations with an antidote type of effect but also of various agents of pathogenetic and symptomatic therapy, depending on the individual condition of the afflicted person. First of all, it should be kept in mind that a marked depression or stoppage of respiration requires prompt measures in the sense of application of artificial respiration (Elam, Clements, Brown, Elton). It should be noted particularly that artificial respiration is more effective than the use of preparations which excite the respiratory center in similar cases. Thus, the timely use of artificial respiration in combination with the use of an antidote and other therapeutic agents can prevent the death of the intoxicated person even after large doses of the toxin. The performance of artificial respiration for a long period of time makes

it possible not only to maintain the function of the respiratory center for a long time but even restores it. Thereby, it should be taken into consideration that artificial respiration is more effective only in case it is carried out by means of special instruments. Hand methods are less effective. Even better results may be obtained through the combination of artificial respiration and administration of oxygen.

As is well known, after injury with organic phosphorus compounds considerable disorders are observed in the patients in the cardiovascular system. In such cases, camphor, caffeine, strophanthin and other agents should be recommended in appropriate doses. However, the use of cardiovascular stimulants alone in the severe cases of intoxication does not produce the desired result. The use of these agents in combination with atropine or other preparations of the antidote type of action is much more effective.

With the aim of reducing and stopping the convulsive paroxysms, the use of anesthetic and narcotic agents is recommended along with atropine. At the same time, the use of such agents which considerably depress the respiratory center (chloroform, morphine) should be contraindicated (Jaques and others). When necessary, the use of glucose, ephedrin, luminal and others is indicated.

Therefore, the use of antidotes in combination with agents

of symptomatic therapy has been made the basis of therapy of intoxication by organic phosphorus compounds. A certain sequence in rendering first aid and treatment may be recommended. First of all, the patient should be removed immediately from the contaminated atmosphere after first putting a gas mask on him. It should be kept in mind that the outcome of the intoxication depends on the ~~type~~ timely use of the antidote and, therefore, ~~e~~ under all conditions (by way of self-help or mutual aid) it is necessary to use a special antidote.

Under conditions where the toxin comes into contact with the mucous membranes (eyes and others) they should be washed out with two percent sodium bicarbonate solution, and in the presence of miosis one or two drops of one percent atropine solution should be instilled into the eyes. At the first opportunity the patient's clothes should be changed.

In mild cases treatment may be limited, chiefly to a single application of atropine (one milligram subcutaneously or by mouth). Pyramidone is used for headaches.

In the more serious cases of intoxication a special antidote, possibly atropine, is injected but in larger doses (one to two milligrams) repeatedly (every four to six hours). In addition, at the same time symptomatic measures are indicated: for excitation, luminal;

for signs of asphyxia, oxygen therapy; of the cardiac agents, camphor, caffeine. It is recommended that conditions of complete rest be created, because the slightest movement aggravates the condition of the patient.

In the severe forms of intoxication the immediate administration of the special antidote or of atropine (see above) is indicated. In parallel with this, in the presence of a marked disturbance or stoppage of respiration, artificial respiration is given, and oxygen is prescribed. Before giving artificial respiration the respiratory tract should be cleaned of mucus and fluid. For the purpose of stimulating cardiac activity caffeine and strophanthin are prescribed. In the case of marked circulatory disorders adrenalin and slow blood transfusion are recommended. The patient should be given rest and subsequent hospital treatment.

The system of treatment of injuries by organic phosphorus compounds presented above is only a tentative one and cannot be considered absolutely perfect.

Fourth Lecture

The Fundamental Principles of Organization of the Work of the MPVO Medical Service in Cases of Mass Attack Against the Population With Organic Phosphorus Compounds

Modern medical service tactics of the MPVO is based on a scientifically grounded system of therapeutic-evacuation care. The principles of stage therapy with evacuation of the patients as indicated and all-possible approximation to the focus of the attack (OP) by qualified and special medical aid with consideration of all the characteristics of the complexified medical-tactical circumstances (A. Ye. Minenko) have been made the basis of this system.

In the event of occurrence of a focus of mass attack against the population, one of the principal and decisive elements in the provision for the therapeutic-evacuation care to patients is a well and properly organized medical classification. It consists of a distribution of the patients into groups which are homogeneous with respect to the following: 1) the nature and severity of the intoxications;

2) the type and the degree of urgency of the medical aid; 3) those with indications for evacuation and groups according to the sequence of evacuation; 4) homogeneous with respect to the method of evacuation and the type of ambulance to be used. Such a distribution of patients provides for the possibility of organization of timely medical care, correct, complete and successive treatment, as well as efficient evacuation of patients as indicated. At the same time, only the correct solution of all these problems can provide for effectiveness in the operation of the MS MPVO /Medical Service of the Antiaircraft Defense/ in eliminating the foci of mass involvement of the population. Medical classification is accomplished at all stages of the therapeutic-evacuation care of patients and should be obligatory, timely, successive, and should contribute to the proper organization of medical care, treatment and evacuation of the afflictec persons. In every individual case the characteristics of medical classification are determined by the medical-tactical circumstances in the focus of involvement and the volume of medical care possible at various stages of evacuation. A compulsory reduction or the possibility of expansion of the volume of medical care at a given stage will directly influence the nature of the classification accomplished.

The following types of medical classification are distinguished (I. M. Timko): 1) intrastation -- the distribution of patients within a given medical institution in accordance with the nature and severity of the affliction; 2) diagnostic -- the determination of the nature, volume and sequence of rendering medical aid to the patient as well as the probable outcome of the affliction of the tentative duration of therapy; 3) evacuation-transportation -- the establishment of a stage of medical evacuation to which the patient should be evacuated for the purpose of further treatment (the place to which he is to be evacuated should be indicated), of the sequence of evacuation (first or second), type of transportation (truck, ambulance, automobile, adapted or unadapted; for the slightly afflicted -- on foot or by automobile), methods of transportation for evacuation (sitting, lying, on the first or second tier).

In the case of mass attack against the population with organic phosphorus compounds medical first aid to the afflicted is given directly in the focus of involvement itself by medical group personnel, among which are the sanitation units (SZ) sanitation brigades (SD) detachments for searching out and manual evacuation of patients (ORVP) as well as by the personnel of groups of other MPVO services. All the population capable of working should be brought

in for this work, and they should work in the focus of involvement under the supervision of a nurse of the search-classification groups (PSG), detachments of medical first aid (OPM). Here, a primary medical classification of the patients is accomplished, a distribution of them into groups in accordance with the sequence and method of evacuation needed from the focus of involvement. It should be emphasized that despite the relative primitiveness of the medical classification under these conditions, because it is even performed by non-medical workers, its part in the matter of saving lives of those affected by organic phosphorus compounds is exceptionally great. Hereby, the efficacy of further medical measures and the possibility of a favorable outcome depend on the speed of rendering medical first aid and evacuation of patients from the area of involvement, the proper selection of the method of evacuation and the timely rendering of medical first aid.

Taking into consideration the particularly high degree of toxicity of organic phosphorus compounds and a number of specific qualities of their effects, it should be considered that the majority of persons affected by these compounds will be seriously afflicted, regardless of their feeling of well-being at any given moment. Therefore, they should be evacuated from the focus of involvement to medical institutions as quickly as possible. The evacuation should be performed by the gentlest type of transportation (litter, ambulance or truck--specially adapted for the transportation of seriously afflicted persons).

The afflicted person himself should remain for the entire time in a comfortable lying position, under calm conditions with a minimal expenditure of efforts and energy. In all cases of injury with organic phosphorus compounds the earliest possible use of the antidote if obligatory.

The volume of medical first aid for persons afflicted by organic phosphorus compounds carried out by mass medical groups (SZ, SD, ORVP, PSG) in the focus of involvement consists of the immediate application of a gas mask to the afflicted person or the replacement of a faulty gas mask (with a preliminary, if necessary, appropriate treatment of the face and observance of all the rules established for such cases) and the administration of the antidote. Outside of the contaminated area a copious irrigation of the mucous membranes of the eyes, nose and mouth is accomplished with water or two percent sodium bicarbonate solution and a partial sanitation-chemical processing with the use of the individual gas casualty kit. In the presence of medical indications it is necessary to stop bleeding, to use artificial respiration, to apply a sterile dressing, to accomplish immobilization, et cetera. After rendering medical first aid the afflicted persons,

where possible, are evacuated directly to the nearest city hospitals of the MS MPVO. In the event they are destroyed or they are too far, the medical first aid can be given in the nearest medical first aid detachments (OPM) as well as in the hospital units for medical aid (SPM).

The extent of medical aid to those affected by organic phosphorus compounds in the OPM, PPM and SPM chiefly consist of the administration of the antidote, the removal of the toxin from the gastrointestinal tract as well as a processing of the mucous membranes of the eyes, mouth and upper respiratory tract; a partial or, where necessary, complete sanitary-chemical processing with degassing of the clothes and footwear. Here, emergency surgical care is given: definitive stoppage of bleeding, surgical operations for vital indications, the application correction and replacement of bandages, immobilization, blood transfusion and infusion of blood substitutes, the administration of tetanus and gas gangrene sera for prophylactic purposes, antibiotics, et cetera. At the same time, emergency therapeutic care is also given: bringing the patient out of the condition of shock, combating anoxemia and asphyxia (oxygen therapy, artificial respiration, et cetera), the

prevention or lessening or the absorptive effect of the toxin, the prevention and control of the phenomena of toxic pulmonary edema, the use of cardiac, symptomatic agents, et cetera. As an obligatory matter, registration of the afflicted persons is accomplished and a- initial medical records are filled in according to the established form. It should be noted that the indicated extent of medical aid is tentative, because it cannot be constant at any stage of medical evacuation but rather is set up depending on the general medical-tactical circumstances which have been built up and can be changed at various periods of eliminating the focus of involvement.

After rendering medical aid in the OPM and SPM those affected by organic phosphorus compounds, according to sequence, are evacuated in accordance with medical indications (evacuation-transporation classification) to the nearest MS MPVO hospitals of the city, and when these are absent, they are evacuated to suburban hospitals of the classification-evacuation base (SEB) by the gentlest method of transportation. Those afflicted by OV arriving by any method at the hospitals of the MS MPVO are subjected in intrahospital (intrastation) classification in the classification-receiving

departments. In the sanitary processing area of the hospitals of the MS MPVO sanitary-chemical processing is given to patients who have not received it at previous stages of evacuation, and their clothes and footwear are sent out for degassing. From the classification-receiving department of the hospital those affected by organic phosphorus compounds are sent to therapeutic departments in accordance with medical indications (diagnostic and prognostic classification) where they are given qualified and specialized medical aid. As a rule, the patients admitted to the hospitals of the MS MPVO, are not subjected to any further evaluation and are given an entire course of treatment in full volume until they recover. However, in individual cases, in the presence of particularly complexified medical-tactical circumstances, the evacuation of part of the transportable patients from the city hospitals of the MS MPVO to SEB institutions may be required.

As a matter of organization of medical care, particularly in the case of mass attacks against the population, a considerable part belongs to the toxic-therapeutic brigades, both those included in the detachments and groups of specialized medical care (OSMP and GSMP) and those which are individually formed.

Highly qualified personnel with considerable practical experience in medical work according to their category and a good supply of drugs, dressing material and other equipment make it possible for toxic-therapeutic brigades to organize a complete specialized aid with the utilization of the latest achievements of medicine. These characteristics of the toxic-therapeutic brigades of the OSMP and GSMP account for the possibility of their personnel accomplishing not only the work within the limits of a special category but also in another, different category, for which the need may arise, depending on specific medical-tactical circumstances which arise. The greater mobility of these groups makes it possible rapidly to organize specialized medical care at various stages of evacuation for the patients. Thereby, the brigades may be sent not only to any hospital institution of the MS MPVO, but in various cases also to the OPM, if the circumstances require it.

In solving problems organization of the MS MPVO special attention should be directed to the specific characteristics of the entire medical service work under conditions of elimination of the consequences of a chemical attack by the enemy. It should be taken into consideration that even in the event of use of only

chemical weapons by the enemy without combining it with other types (demolition, fragmentation and incendiary bombs, atomic and bacteriological weapons), which can hardly occur, patients will be admitted to the hospitals of the MS MPVO and medical aid stations with burns, injuries and possibly, other patients along with those affected by organic phosphorus compounds. The latter circumstance considerably expands the volume and complicates the therapeutic-evacuation work. The need arises for a strict division of persons afflicted by droplet organic phosphorus compounds, which present a danger to those around, from the other categories of patients. This leads to the need for organization of a continuous-flow system of care at the medical aid stations and in the hospitals without crossing of the corresponding lines, whereby the part played by the receiving-classification departments of the OPM, SPM and hospitals of the MS MPVO increases particularly.

Medical institutions should be provided with special medical equipment for caring for persons afflicted by organic phosphorus compounds (in the dressing and operating rooms individual tables, instruments, et cetera should be set apart), as well as

with facilities for antichemical protection of the personnel. In the receiving-classification departments and in the sanitary processing rooms of the medical institutions the personnel should work in protective clothing and gas masks. For the proper accomplishment of all the measures mentioned above special training is required for the entire personnel of the groups and institutions of the MS MPVO and training of it in the characteristics of medical work under conditions of elimination of consequences of chemical attack by the enemy.

Sanitation-Chemical Examination, Protection of Water and Food Products after Contamination by Organic Phosphorus Compounds

General Problems of Sanitation-Chemical Examination

In a chemical attack food products and water may be subjected to the effect of war gases. Here, the contaminated food products become dangerous for man and may be the source of intoxication of him. The degree of intoxication depends on the properties of the food product itself and on the nature of the packing of the latter. As a result of an examination made food products may be divided into the following groups according to the degree of contamination:

1) products which are in reliable and intact shelters (protected storehouses, refrigerator chambers, tightly sealed containers, et cetera);

2) products which do not have any external signs of contamination

but which are in the immediate vicinity of contaminated premises or contaminated territory;

3) products which are definitely contaminated.

Products belonging to the first group are considered arbitrarily non-contaminated. However, the use of them is possible only after decontamination of the territory and outer surfaces of the protected premises or containers with subsequent check examinations of samples of these products in the laboratory.

Water and food products can be contaminated: 1) by means of the military use of war gases; 2) by means of a diversionary attack. With any of the methods of chemical attack used under current conditions all open sources of water and reservoirs, food products and semifinished products kept at storehouses, bases, food enterprises, under domestic conditions as well as during transporation may be subjected to the effect of organic phosphorus compounds.

Work on the examination of water, food products and fodder for the detection of war gases is entrusted to the medical, veterinary as well as the mercantile and food services of the MPVO.

Measures for the examination of water, food products and fodder consist of the following: 1) the determination of the degree of contamination depending on the nature of the chemical agent and the conditions under which the water and food products are kept; 2) solution of the problem of measures to be taken with respect to the water and food products which are undoubtedly contaminated even without chemical analysis; 3) the taking of samples for making chemical analyses of water, food products and fodder suspected of contamination; 4) the proper selection and shipping of the samples taken (if the circumstances require this) and the performance of the analysis itself; 5) the making of one decision or another on the basis of the data of the analysis with respect to water, food products and fodder suspected of contamination; 6) the rendering of conclusions concerning the possibility of utilization of food products, semifinished products and fodder contaminated with war gases by people and animals as well as the recommendations for possibilities of degassing, utilization of them or the need for destruction of them. Large batches of food products can be destroyed only after repeated and unsuccessful degassing or when it is impossible.

Laboratories (city, inter-rayon and installation) are included in the medical service of the city MPVO. The city and inter-rayon laboratories include three departments: radiometric, sanitation-chemical and bacteriological. The installation laboratories may have one, two or all three of these departments.

The detection of war gases as well as the examination of water, food products and the rendering of a conclusion concerning their suitability are included in the problems of sanitation-chemical department of the MS MPVO laboratory. For this purpose, the department of the sanitation-chemical examination board is equipped with all the necessary reagents, apparatus and facilities for personal protection.

The mercantile and food services of the MPVO organizes control units at all the food installations (bases, storehouses, refrigerator set-ups, elevators, meat combines, stores, delicatessens, dining rooms, et cetera). The control unit consists of four people, and their number is determined by the chief of the MPVO installation. The control units are obliged, with the occurrence of foci of involvement at the installation, to examine food products, water, raw material, semifinished

products and to take samples of products which are contaminated or suspected of contamination, being guided by rules of selection of samples thereby.

The samples of food products, water, raw materials, semifinished products which are taken for laboratory examination by workers of the control unit are sent to the installation laboratory of the MS MPVO (of the given installation), to the city or inter-rayon laboratory organized at the sanitary epidemiological station. In connection with this, an important part is played by medical workers who are set apart for training the personnel of the control units. In the performance of exercises special attention should be given to the acquisition of good practical habits by every worker in the control unit for taking samples, with the observance of all the rules of taking samples, of taking measures of personal protection, as well as for filling in the necessary records and sending the samples taken to the laboratory.

It is most expedient to bring in medical workers of food and mercantile enterprises as well as physicians of the sanitary epidemiological stations for training the control units.

Samples of fodder for investigation are sent to the laboratory of the veterinary service of the MPVO.

For the purpose of taking measures for the decontamination, utilization or destruction of food products contaminated by war gases special detachments of the mercantile and food services of the MPVO are organized in the city and are given the appropriate training. The personnel of the control units may participate in these measures.

Without the sanitary-chemical examination the utilization and issuance of food products is prohibited when there is the slightest suspicion of contamination in storehouses, public dining room enterprises and food stores.

The Order of Taking Food Product Samples

For the purpose of solving the problem of the degree of contamination laboratory examination should be made. For this purpose the personnel of the control unit takes samples of food products which are contaminated and suspected of contamination. It should be kept in mind that in the infection of the same food product with BO, OV or BRV, the food product samples are taken first for examination for bacteriological contamination, preparing the necessary sterile glassware for this purpose. Then, the

samples are taken for determination of the presence of OV or BRV [war gasses or military radioactive substances].

For the rapid determination of the type of OV used samples for analysis are taken which have traces of the weapons used on them (drops, dust, et cetera) or from places where definite signs of contamination are found (spots made by drops). When there is a suspicion of contamination of food products which are in a packing container or in a protected pack, the selection of samples is made in the following way: first, samples are taken from the surface of the pack (packing or shelter) and then decontamination of the surface of the pack (or room) is accomplished. Only after this are samples of food products taken. If there are no signs of contamination the samples of food products are taken from no less than four or five areas of the suspected site of contamination.

The samples are taken with cotton tampons on a stick or wire from the contaminated surface of the container. Samples of grain, cereal and other loose products are taken by means of an iron trowel from a depth of one to two centimeters and in a quantity of 100 to 200 grams and are put into glass jars. The samples of the loose products which are in a sac container

are taken with a metal sound from the surface layer (directly under the sac), and products which are kept in a box are taken from the surface in contact with the contaminated wall of the box. Packed products are taken for examination in quantities of two or three packs from the outer layer. Samples of animal fat, oleomargarine, are taken by means of cutting the surface layer in a thickness of 0.5 centimeter. Liquid and semiliquid products (vegetable oil, milk, beverages) are taken by means of a siphon (glass tubes) from the surface, from the bottom, and after careful mixing. For the purpose of investigating baked bread the samples are taken as entire loaves. Samples of meat are taken by means of cutting a section of the surface layer having a total weight of about 400-500 grams. Samples of water for laboratory analysis are taken in quantities of no less than 0.5 and no more than three liters, of necessity at a place from which it is subsequently proposed to take water for drinking purposes (or for external use). Water is taken from wells with clean glassware following a careful mixing (water which has first settled in the pipes is drained off for 10 minutes).

Taking into consideration the physicochemical properties of

organic phosphorus compounds (no odor or color, high degree of toxicity and a comparatively rapid hydrolysis), workers in the control unit should provide for taking samples and shipping the samples in the shortest possible time. With the arrival of the food products or water which is contaminated or suspected of contamination the analyses should be performed in short order. After taking the samples the instruments are degassed with cotton tampons moistened in alkaline solutions. The cotton tampons are burned or are poured over with degassing solutions for three to four hours.

Samples taken for laboratory examination are recorded on a special blank sheet (for examples of the blank sheet data see Table 1).

Then, a careful check is made on the condition of stoppage of jars and test tubes. The samples are packed in a special box with an accompanying blank (an example of the form of the blank is shown in Table 2) and are sent to the laboratory of the MS MPVO (installation, inter-rayon or city).

When there are stores of food products or water under domestic conditions which are contaminated or suspected of contamination with OV, the samples should be sent to the

nearest MS MPVO laboratory. Before obtaining the results of the analysis the food products and water should not be used.

If from the laboratory result the food products are considered unsuitable for use as food they are subjected to degassing, destroyed or utilized (if possible) under the supervision of the appropriate staffs of the mercantile and food services of the MPVO by the personnel of the installation groups and with checking by staff workers and appropriate medical service activated units of the MPVO.

The Sanitary Examination of Water and Food Products

When organic phosphorus compounds enter water, its external appearance is unchanged as a rule. This is associated with the physicochemical properties of these compounds (a liquid which mixes well with water). While they possess a very slight ethereal odor they do not give the contaminated water any perceptible odor. Therefore, the organoleptic examination of the water under such conditions does not give anything to the sanitary-chemical examination. After contamination by large quantities of these substances the acidity of the water is changed, and the concentration of the hydrogen ions is increased. No other changes can be found. The duration of the contamination

of water by organic phosphorus compounds is determined by the periods of their hydrolysis. However, it should always be kept in mind that the end of hydrolysis cannot serve as a criterion for evaluating the suitability of water for drinking and preparing food, because as a result of hydrolysis products which are toxic for the body remain (fluorine, HCN and others). The periods of hydrolysis of organic phosphorus compounds are different and depend on their concentration in the water and the temperature (depending on the concentration, the duration of hydrolysis can vary from three to 50 days).

Table 1

Information About Samples Taken

№ пп (1)	№ пробирки, банки, пакета-указанием характера упаковки (2)	Место отбора проб (наименование склада цеха, № стеллажа и т. п.) (3)	Дата отбора проб, с указанием часов и минут (4)	Наименование продукта, из которого взята проба (5)	Кем отобрана проба и его подпись (6)	Дата направления пробы и лабораторию с указанием названия лаборатории (7)

KEY: 1) No. of item; 2) No. of test tube, jar, pack with indication of the nature of the packing; 3) Site of samples taking (name of storehouse, shop, no. of frame, etc.); 4) date of taking samples, with indication of hours and minutes; 5) name of product from which sample was taken; 6) by whom sample taken and signature; 7) date of sending sample to lab with indication of name of laboratory.

Table 2

Accompanying Blank

Год, м-ц, число и время предполагаемого заражения (1)	М-ц, число и время отбора проб (2)	М-ц, число и время отправки проб в лабораторию (3)	№№ пробирок, банок, пакетов (4)	Наименование продуктов, из которых взяты пробы (5)	Цель исследования (6)	Адрес объекта, где производился отбор проб (7)	Время доставки проб в лабораторию и фамилия лица, доставившего пробы (заполняется сотрудником лаборатории) (8)	Примечание (9)

KEY: 1) Year, month, day and time of suspected contamination; 2) Mo., day and time of taking samples; 3) Month day and time sending samples to laboratory; 4) Nos of test-tubes, jars, packs; 5) name of products from which samples were taken; 6) aim of examination; 7) address of installation where samples were taken; 8) time of delivering samples to the laboratory and last name of person delivering samples (filled in by laboratory worker.

Therefore, neither organoleptic examination nor chemical analysis give adequately clear-cut data concerning the presence of these compounds in the water. Therefore, the detection has to be made by means of special tests. When even insignificant quantities of these substances are present in the water the water should be degassed and purified of their decomposition products. The method of purification of water contaminated with organic phosphorus compounds is based on an acceleration

of their hydrolysis in an alkaline medium. For this purpose the water is subjected to liming. Here, the water purification proceeds more quickly the more lime is added. The optimum quantity of the latter is determined by the degree of hydroxide alkalinity, which should not be any less than 0.8 milligram per equivalent. In the hydrolysis of organic phosphorus compounds toxic decomposition products are formed which, by means of calcium hydroxide, produce salts which are poorly soluble in water, which are precipitated and removed along with the lime sediment. After the conclusion of hydrolysis biological tests should be performed. As control tests the determination of the activity of blood cholinesterase and the pupillary reaction (miosis) should be determined after the administration of a drop of the water being tested into the conjunctival sac.

In the contamination by organic phosphorus compounds consideration should be given to the depth of penetration of food products in addition to the physicochemical properties of these compounds and the methods of their application. When OV comes into contact with an oil it contaminates its entire layer, but the greatest quantity of the agent settles to the bottom. The external

appearance of the food products contaminated with organic phosphorus compounds does not show anything characteristic. Only after the contamination of meat by droplets of these agents are grayish patches formed on its surface which do not disappear even after washing and cooking the meat.

Detection of organic phosphorus compounds in food products may be accomplished by the glass etching test, the alizarin zirconium test, and other methods. Here, it should be kept in mind that the chemical determination usually is made from the decomposition products. For example, sarine is determined by its fluoride ion, which is normally present in the water and food products. Therefore, when the detection is performed this circumstance should be taken into consideration. For this purpose, organic solvents are used which extract only fluorine contained in the sarine. The determination of tabun is also made after it is extracted from the contaminated food product or water by an organic solvent and with respect to its CN ion.

After the degassing of contaminated food products, a biological check should be made for the completeness of degassing. For this purpose, the degassed products are fed to experimental animals, and an observation is made of the

condition and behavior of the latter, and the cholinesterase activity is determined. An extract obtained from extraction of the food products by the solvent after degassing should be introduced into the conjunctival sac of the animal for the purpose of determining miosis which occurs in the presence of even the slightest quantities of organic phosphorus compounds.

Protection of Food Products and Water

Organic phosphorus compounds constitute the greatest danger, because they possess a high degree of toxicity and are difficultly determinable organoleptically. The latter fact is of great importance, because the presence of the toxin may remain unnoticed, which creates the danger of intoxication not only after consumption of such products as food but also from contact with them. In turn, degassing of the food products is frequently associated with considerable difficulties and sometimes it is entirely impossible. Therefore, the principal measure for preserving food products after a chemical attack is a protection of them, which amounts primarily to the fact that the possibility of entrance of the toxin into the food products is presented. The food products and prepared food are best kept in metal and glass containers. Wooden containers (boxes, barrels, vats)

which do not have any cracks and which are tightly sealed may be used successfully. In the event of a chemical alarm it is recommended that this type of container be covered over with canvas or with sacs. In order to protect wells from contamination with war gases they should be covered over with a tightly fitted wooden cover. A well tamped down layer of clay 1.5 meters in width and 20 centimeters in depth is arranged in the soil around framework wells.

It should be kept in mind firmly that it is much more difficult to degas food products than to protect them against possible contamination. Therefore, only measures taken in time for the antichemical protection of food products and water completely provide for the preservation of food products in the case of a chemical attack.

Antichemical Protection against Intoxication by Organic Phosphorus Compounds

Individual Protective Facilities

In principle, protection against organic phosphorus compounds is no different from protection against other well-known war gases. Combined-arms, civilian and insulating gas masks are used in the local antiaircraft defense system.

Both the combined-arms and the civilian gas masks consist of a gas mask cannister and a face portion. There is a gas mask bag for keeping and transportation. The cannister serves for the purification of contaminated air by means of filtration through absorbers (filter mask), and the facial portion of the mask is for bringing the purified air to the respiratory organs and for the protection of the eyes. The face portion of the gas mask consists of facepiece with goggles, a valve box with inspiratory and expiratory valves and a connecting tube. Before the advent of the highly toxic substances of the organic phosphorus type all the gas masks had only a single expiratory valve in the valve box. Given this, the possibility of intoxication with highly toxic substances was not excluded because of the possibility of inleakage during inhalation of air. For this reason, two expiratory valves are now used in all gas masks. Thus, for

example, in the valve box of the face portion of the civilian gas mask there is an upper expiratory valve and a lower valve, which is protective and serves for reducing inleakage under the mask through the upper expiratory valve. The space between the upper and lower expiratory valves is called the "physiological chamber".

In protection against organic phosphorus compounds the selection of the proper size face portion of the gas mask is of particular importance. However, no matter how well the face portion fits on the head, an obligatory condition is checking of the quality of the mask in gas chambers specially equipped for these purposes. Therefore, all activated units of the MPVO must adhere strictly to this rule in obtaining gas masks. In addition to filter gas masks insulating gas masks are used which operate on the principle of complete isolation of the respiratory organs from the environment, whereby respiration occurs with the use of the oxygen in the mask.

Skin Protection Facilities

Taking into consideration the fact that the organic phosphorus compounds in the liquid and vapor states are capable of penetrating through the skin, protection is needed not only for the respiratory organs but also for the entire human body. For this purpose, protective mantles, overalls, protective aprons, socks, rubber boots and gloves are used. Here, it should be kept in mind that complete protection is achieved only by means of overalls, which completely insulate a person from the intoxicated atmosphere.

Protective mantles and aprons cannot give complete protection, which should be kept in mind in working in foci of involvement by organic phosphorus compounds. Therefore, in protecting the human body against these compounds a special part is played by skin protection facilities, along with the insulating measures, made of filtering material--fabrics dipped in special compositions. Among them are impregnated uniforms, underwear and other clothes. Aside from the authorized allowances of supplies for skin protection, handy measures may be used made specially for this purpose and ordinary clothing: raincoats, mantles, overcoats made of leather or heavy cloth, as well as clothes made of ordinary fabric. For protection against contaminated areas, particularly in evacuating the population from a contaminated locality, and in rendering medical aid to the afflicted, galoshes, rubber boots, footwear covered with paper and other agents may be used depending on their availability and the local conditions.

Collective Protective Measures

Shelters which are set up and outfitted in the cellars of houses, industrial and public buildings, are used as collective protective measures for the population against war gases. For the purpose of providing protection every shelter should be equipped in the antichemical respect. Among the main elements of antichemical equipment of the shelter are the following: tight sealing, the use of filtered air-conditioning and oxygen-regenerative apparatuses as

well as air locks. Oxygen-regenerative apparatuses are not used in all shelters. In analyzing the protection against organic phosphorus compounds in group structures, it should be kept in mind that in these cases hermetic sealing acquires particularly great importance. If it is carried out adequately, then, after closure of all doors and manholes and after starting the filtered air-conditioning apparatuses an excess of air pressure is created in the shelter by comparison with the outside , which is the main condition for the protection of persons in the shelter against organic phosphorus compounds. Another condition is the careful checking of the operation and timely replacement of used up filter-absorbers, which provide for the purification of the air supplied to the shelter. In addition, when the shelter is filled with people the doors of the air locks should be opened in turn: first, the protective-sealing door is opened, and a certain number of persons enter the air lock; then, this door is closed, and the sealing door is opened directly into the shelter. Observance of these rules in the event of the presence of organic phosphorus compounds in the air is extremely essential. It should also be kept in mind that when the shelters are filled, people should take off their outer clothes before entering them, particularly in those cases where they have been in a locality severely contaminated with organic phosphorus compounds for various reasons.

Sanitary Processing

For the purpose of removing or neutralizing organic phosphorus

compounds sanitary processing of the population which is in the chemical focus of involvement is performed; this consists of a careful washing of areas of skin on which the toxin has fallen, with water and soap or other alkaline solutions. The water practically does not lessen the toxic effect of the organic phosphorus compounds which have fallen on the skin. Soap is of a certain importance for reducing the toxic effect of these agents (green soap or laundry soap) because it contains alkali. Under the influence of alkaline ~~al~~ solutions or ointments the organic phosphorus compounds are broken down and do not constitute a threat to man. Such processing may be carried out the by population itself by way of self-help or mutual aid, directly on leaving the contaminated focus under domestic conditions, as well as by the personnel of the sanitation units (SU), sanitation brigades (SB), detachments for seeking out and manually evacuating the afflicted (OMVP), medical units, self-protection units, medical groups or detachments at installations. Taking into consideration the high degree of toxicity of organic phosphorus compounds the time factor, which determines the success of sanitary processing, is of importance. The earlier the incomplete sanitary processing is carried out the greater its effect. Complete sanitary processing includes washing of the entire body under a shower with soap, degassing of clothes in degassing chambers and of footwear by means of decontaminators, washing of the eyes with alkaline (sodium bicarbonate) solutions and rinsing the oral cavity.

All persons affected, showing signs of intoxication or combined injuries, are sent for sanitary processing to activated medical service units of the MPVO (decontamination departments of the OPM, receiving-classification departments of the SPM, sanitary processing rooms of hospitals) after medical first aid has been given by the sanitation brigades (or in the course of self-help or mutual aid). With a small number of patients it is most expedient to organize the sanitary processing of them in the SPM, where first aid by a physician can be given or in a city hospital. The population which is to be given sanitary processing and which is without wounds or injuries, that is, those who do not need qualified medical aid after the sanitary processing, should be sent to the hospital decontamination stations (SOP). The latter are organized by the service for sanitary processing of persons and decontamination of clothes in the MPVO at the bath-house and in the sanitary processing rooms (with the exception of the sanitary processing rooms of the therapeutic institutions). In the hospital decontamination stations a complete or partial sanitary processing may be performed for the patients and medical aid can be given for minor injuries. For this purpose, the medical service of the rayon or city MPVO sends one or two nurses to each SOP with the aim of checking on the quality of the sanitary processing as well as for rendering medical aid for minor injuries. Medical workers in the SOP should be well acquainted with the locations of the nearest medical institutions (OPM, SPM, hospitals) and the travel routes there.

In consideration of the high degree of toxicity of the organic phosphorus compounds, measures should be taken so that the sanitary processing of people be accomplished in the shortest possible time after the contamination. This is assured by a high degree of preparedness of the units and institutions of the MPVO, primarily of the medical service, and the sanitary processing services for people and clothes decontamination of the MPVO as well as by a high level of training of the population and personnel of the mass units (sanitation brigades, ORVP). During the sanitary processing of people affected by organic phosphrous compounds the necessary measures should be taken for the protection of personnel working in the SOP, ODO-OPM, PSO-SPM and sanitary processing rooms of hospitals. Therefore, the quality of the exercises performed by the medical personnel as well as by the instructors of the DOSAAF [All-Union Voluntary Society for the Promotion of the Army, Air Force and Navy] and Red Cross in training the population and mass unit personnel in the rules of utilization of individual protection facilities for people against war gases and for rendering urgent aid to those affected directly in the focus of involvement. In the performance of such exercises attention should be directed to training the entire population in good practical habits for using both the authorized and handy measures for protection, rendering self-help and mutual-aid for intoxications.

Degassing

This is the name for the totality of operations which have

the aim of decontamination of installations contamined with war gases. Degassing may be performed by the chemical method by means of degassing agents; by the mechanical method, by removing the surface layer or by the creation of an insulating covering for the contaminated area; by the physical method, by removing the OV with the aid of solvents or evaporation; by the physicochemical method, by sorption and hydrolysis of the OV.

Such measures are used as decontaminators which react quickly with the OV [war gas] and convert it into harmless compounds. Ammoniated-alkaline solution (degassing solution No 2), which contains two percent sodium hydroxide, five percent monoethanolamine and 20 percent ammonia, is of special importance for the decontamination of technical equipment, transport and other objects contaminated with organic phosphorus compounds. For the preparation of it ammonia water is used with a concentration of ammonia of no less than 22 percent, sodium hydroxide and monoethanolamine, which contains no less than 80 percent of the basic substance.

These substances are among the authorized degassing agents with which the units and activated units of the MPVO are equipped. Aside from the authorized degassing agents, the so-called local degassing material may be extensively used; this includes the following: clay, lime, lime sediment, degassing lime material, as well as wastes and semifinished industrial products, etc. Thus, for example, slaked and unslaked lime, ashes, caustic, carbonate and sulfite alkalis, etc.

may be used.

Under the local PVO conditions, various substances and technical facilities may be used for the degassing of streets, sidewalks, buildings, transport, small metal articles, skin protection facilities, clothes, etc., depending on the material of the object and the OV used by the enemy. For the purpose of spreading loose degassing material over a locality the locality degassing instrument (PDM), the portable sowing degassing instrument (SVDP), the community sandblasting machines and machines for spreading fertilizer. Self-protection groups have sieve-carriers on supply for this purpose. By means of these technical facilities the degassing of a locality contaminated with organic phosphorus compounds may be accomplished by means of slaked and unslaked lime, ash wastes and other agents.

For the purpose of degassing surfaces contaminated with organic phosphorus compounds by means of a suspension of chemically active agents (slaked lime) or by ammonia solutions, motorized pouring stations (ARS), irrigating machines (PM-6 and PM-8) and others are used. For the purpose of degassing vertical surfaces adapted irrigating machines, cesspool pumps, the "Pioner", portable degassing instruments "RDP", as well as certain construction machines and instruments used in plastering and painting buildings, and agricultural sprayers may be used.

In the organization of the operations of the activated medical units in mass attack foci, the problems of technical equipment,

transportation, various instruments and clothes acquire special importance. For the purpose of degassing public city transportation special structures are erected: transport degassing stations (STS) of transport degassing stations of the simplified type--degassing areas (DP). For the purpose of degassing transport as well as metal articles, instruments and other objects the following methods are used: rubbing with brushes moistened in solutions of degassing agents, processing with aqueous pastes and suspensions of degassing agents, spraying with solutions of degassing agents, washing with solvents, steam and hot water.

Degassing of transport, metal items, instruments and other objects is carried out in the following order: if the type of war gas has not been determined the contaminated articles are treated with degassing solution No 1 (five to eight percent DT-6 solution in dichloroethane, or 10 percent DT-2 solution in dichloroethane); then with degassing solution No 2 (see above); if the type of OV has been determined, solution No 1 is used for degassing substances of the mustard gas and lewisite type, and solution No 2, for degassing organic phosphorus compounds. For the purpose of the latter solutions of sodium sulfite, aqueous alkali solutions, alkaline emulsions as well as industrial wastes containing alkalis are used.

Clothes, footwear and antichemical protection facilities contaminated with organic phosphorus compounds are degassed with a steam-ammonia mixture, steam-air-ammonia mixture, by boiling,

successive treatment with hot air and steam (combined method) as well as with hot air.

In the MPVO system degassing of clothes is accomplished in specially outfitted structures, called clothes degassing stations (SDO). The technical facilities for degassing clothes with steam-ammonia mixtures, steam-air-ammonia, hot air and steam are the all-purpose chambers (UK-55) as well as adapted chambers of the Levinson-Chernoshchekov, Pogorzhel'skiy, Krupin, Rubner types and the Grum-Grzhimaylo lumber-drying chambers. Degassing by boiling is accomplished in special bucking apparatuses (BU-4) as well as in handy facilities (cans, vats, etc.).

The essence of degassing with steam-ammonia mixture is that the steam, heated to a temperature of 98-100°C and passing into the mixture with ammonia through the contaminated clothes, hydrolyzes the OV and converts them into non-toxic substances. By this method it is possible to degas cotton, linen, woolen, cloth and silk fabrics as well as articles made of rubber contaminated with all the well known OV, including the organic phosphorus gases. Degassing by the steam-air-ammonia mixture consists of the treatment of the contaminated clothes with hot air containing a relative humidity of 100 percent and with a certain quantity of ammonia. By this method all clothing can be decontaminated with the exception of articles to which drying oil has been applied. Degassing by boiling is based on hydrolysis reactions of the OV in water or aqueous

solutions of sodium bicarbonate and ammonia and is used for degassing all kinds of cotton and rubber articles. Woolen, cloth, leather, and cotton and felt articles cannot be degassed by boiling. Degassing with hot air is based on the evaporation of persistent OV from the contaminated objects. In view of the duration of the process this method is used only in those cases where there is no possibility of carrying out the decontamination by other methods.

Detection

This is the term for the qualitative or quantitative determination of OV on contaminated objects. Detection may be accomplished directly in the locality, by the so-called "field detection facilities", or in MPVO laboratories which have been specially organized for this purpose. For the purpose of determining war gases directly in a locality (in the air or on various objects) chemical reconnaissance instruments are used (PKhR, UAI), in which there are special detection tubes. These instruments are based on the utilization of the chemical reactions of the OV with certain substances (indicators). Each indicator tube in the instrument has certain identification markings which indicate which type of OV can be determined by means of it. On aspirating contaminated air through it, the tube filler changes its original color. Thus, for example, with the aspiration of air contaminated with tabun or with hydrogen cyanide through the indicator tube itse filler is colored pink. In the local MPVO system the reconnaissance groups, which are organized

by the MPVO staffs in areas, cities, installations and in the MPVO services, are equipped with chemical reconnaissance apparatus. The field method of detection is only preliminary and needs careful subsequent checking. Therefore, a network of special laboratories created at the already existing laboratories of scientific research institutes, higher institutions of learning, laboratories of industrial enterprises and institutions is organized for the complete detection of the OV within the local PVO (antiaircraft defense) system. They are divided into city, rayon and installation laboratories of the MPVO as well as laboratories of the MPVO medical and veterinary services. The laboratories which are to be organized for solving problems of antiradiation and antichemical protection solve the main problems in determining the presence of OV in a locality and structures of various kinds, determining the completeness of decontamination, the quality of the degassing agents and protection facilities. The medical service laboratories which are to be organized at food installations and medical service institutions are given the main problem--the determination of OV in food products and water; the veterinary service laboratories--the determination of OV in fodder and water. Methods of detection of war gases are given in special instructions.

BIBLIOGRAPHY

(Only the bibliography used in writing the lectures has been given).

1. Vayl' S. S. Pathological Anatomy of Injuries Produced by War Gases. Leningrad, 1958.

2. Kagan Yu. S., Makovskaya Ye. I. Self-referenced Reports of the Kiev Institute of the Hygiene of Labor and Occupational Diseases. Kiev, 1956.

3. Kagan Yu. S., Makovskaya Ye. I. Proceedings of the Twelfth All-Union Congress of Hygienists, Leningrad, 1956.

4. Kagan Yu. S., Makovskaya Ye. I. Fiziologicheskiy zhurnal AN UkrSSR /Physiological Journal of the Academy of Sciences of the UkrSSR/, 1957, III, No 3 (77).

5. Makovskaya Ye. I. Proceedings of the Anniversary Scientific Conference of the Institute of the Hygiene of Labor of the Academy of Medical Sciences USSR, 1957. "The Organization of Medical Care in Cases of Mass Attacks Against the Population" (edited by A. Ye. Minenko), Kiev, 1957.

6. Sazonova N. A., Vashkov V. I., Volkova A. P. Works of the Scientific Research Disinfection Institute, 1954, No 8 (188).

7. Sartori M. Russian Translation. Uspekhi khimii /Achievements of Chemistry/. No 1, XXIII, 1954.

8. Smirnov G. O., Turpayev G. M. Report of the Institute of Animal Morphology of the Academy of Sciences USSR, 1949.

9. Spynu Ye. I. Self-referenced Dissertation, 1953.

10. Spynu Ye. I. Pharmacology and Toxicology, 1957 (1956 appendix).

11. Yareshko-Brakhnova I. T. Proceedings of the Scientific Session of the Kiev Institute of the Hygiene of Labor and Occupational Diseases, Kiev, 1953.

A. Provisional Instructions for the Work of Control Units at Food Installations. Moscow, 1956.

B. The Regulations for Control Units in Protecting Food Products Against the Effect of War Gases, Radioactive Substances and Bacterial Contamination at Food Installations. Moscow, 1956.

C. Training Program for Control Units on Protection of Food

Products Against the Effect of War Gases, Radioactive Substances and Bacterial Contamination at Food Installations. Moscow, 1956.

12. Aldridge W. Bioch. Journ. 46 (456), 1950.

13. Aldridge W. Bioch. Journ. 53, (117), 1953.

14. Askew B. Brit J. Pharmacol. Chemother. 11, No 4, (417), 1956.

15. Barnes J. Chem. Industry, No 17, (478), 1954.

16. Bloch H. Helvet. chim. Acta 26, (733), 1943.

17. Boursnell J., Webb E. Nature 164, (875), 1949.

18. Brauer R., Hodge H. Fed. Proc. 6, (311), 1947.

19. Derobert M. Annal. de med. biol. XXX, No 1, (32), 1950.

20. Domenjoz R. Schw. Med. W. 50, (1282), 1946.

21. DuBois K. J. Pharm. Exp. Therap. 95, (79), 1949.

22. Elam J., Clements J., Brown E., Elton N. U. S. Armed Forces Med. J. 7, No 6, (797), 1956.

23. Epstein M., Freeman G. Proc. Soc. Exptl. Biol. Med. 92, No 4, (660), 1956.

24. Euler H., Svanberg O. Fermentforsch. 3, (33), 1920.

25. Friedmann A., Himvith H. Am. Journ. Physiol. 153, (121), 1948.

26. Grob D. Bull. J. Hopk. Hosp. 87, 2, (75), 1950.

27. Grob D. JAMA 44, No 21, (10176), 1950.

28. Grob D. Arch. Exper. Path. Pharmacol. 223, (953), 1954.

29. Grob D. Arch. Internat. Med. 98, No 2, (221), 1956.

30. Grob D. U. S. Armed Forces Med. J. 7, No 6, (781), 1956.

31. Hartly B., Kilby B. Nature 166, (784), 1950.

32. Harvey, Du-Bois K., Dull J., Salerno P., Cook G. Journ. Pharmac. Exp. Ther. 75, (79) 1949.

33. Hawkin R., Mendel B. Brit. Journ. Pharmac. 2, (173), 1947.

34. Heymans G., Pochet A., Van Houtte H. Arch. Internat. pharmacodyn. 104, No 3-4, (293), 1956.

35. Holmes K. Proc. Roy. Soc. Med. London, 46, No 10, (799), 1953.

36. Holmstedt B. Acta physiologica Scandinavica 25, Suppl. 90 1951.

37. Jansen E., Nutting M., Jang R., Balls A. Journ. Biol. Ch. 175, (189), 1949.

38. Jaques R., Bein H., Meier R. Schw Med. W. No 34, (1096), 1957.

39. Jones H., Meyer B., Karel J. Journ. Pharm. Exp. Ther. 24 (215), 1948.

40. Kahlson G., Uvnas B. Scand. Arch. Physiol. 78, (40), 1938.

41. Karzmar P. Quoted by R. Zh. Biologiya /Biology/, No 3, 4158, 1954.

42. Kempl H. Arch. Exp. Path. Pharmacol. 223, 1954.

43. Koelle G., Gillman A. Journ. Pharmac. 95, 11, 1949.

44. Kondritzer A. U. S. Armed Forces Med. J. 7, No 6, (791), 1956.

45. Kramer D., Gamson R. Analytic. Chem. 29, No 12, (21), Dec. 1957.

46. Krop S., Kunkel A. Proc. Soc. Exper. Biol. Med. 86, No 3, (530), 1954.

47. Loomis T. J. Pharmacol. Exp. Therap. 118, No 1, (123), 1956.

48. McNamara B. et al. J. Pharmacol. Exp. Therap. 110, (232), 1954.

49. Mackworth J., Webb E. Bioch. Journ. 42, (91), 1948.

50. Mazur A., Journ. biol. Ch. 164, (271), 1946.

51. Mazur A., Bodansky O. Journ. biol. Ch. 163, (261), 1946.

52. Modell N., Kropp I. J. Pharmacol. Exp. Therap. 88, 1, (39), 1946.

53. Nachmansohn D., Feld E. Journ. biol. Ch. 161, (215), 1947.

54. Naeve W. Chem. Zbl. No 7, (179), 1957.

55. Naeve W. Arch. Toxicol. 15, (167), 1955.

56. Needham J., Dixon M. Nature 158, 432, 1946.

57. Reinl W. Archiv für Toxicol. 16, (158), 1956.

58. Rhower S. JAMA 144, No 2, 1950.

59. Ripper W. Ent. Res. 40, No 4, (481), 1950.

60. Siedek H., Tholler H. Arch. Int. Pharmacodyn. 91, (194), 1952.

61. Webb E. Bioch. Journ. 42, 96, 1946.

62. Wilhelmi G., Domenjoz R. Arch. Int. Pharmacodyn. 321, 151.

1288

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